The New England
Journal of Medicine

Copyright, 1940, by the Massachusetts Medical Society

VOLUME 222 JUNE 6, 1940 NUMBER 23

BLOOD-PHOSPHORUS STUDIES IN RHEUMATIC FEVER*

NATHAN EPSTEIN, M.D.,† AND FRANCIS C. McDONALD, M.D.‡

BOSTON

SEVERAL years ago it was noted that many children hospitalized with acute rheumatic fever had been attending our outpatient clinic for months before the appearance of symptoms definitely attributable to their disease. During this period the presenting signs and symptoms were chronic fatigue and failure to gain weight. The occurrence of chronic undernutrition prior to the onset of the symptoms of rheumatic fever stimulated closer analysis of this factor. In the group of patients studied, signs of malnutrition were common. This was attributed to diets inadequate in proteins, minerals and vitamins and relatively rich in carbohydrates, maintained over long periods. One of the essential elements which was deficient was phosphorus. The known relatively high requirement of phosphorus for optimal growth and its role in muscle metabolism prompted an investigation of its content in the blood of a small group of patients.

For the determination of phosphorus the method of Tisdall[1] was used in the earlier part of the study; however, 70 per cent of all the analyses were made with the colorimetric method of Fiske and Subbarrow.[2] Analyses were performed on the bloods of 38 patients. The samples were taken before breakfast, and the examinations were started within half an hour of the drawing of the blood. Analyses were made of the inorganic phosphorus and the total phosphorus of the serum, and of the phosphorus in the alcohol-and-ether-soluble and acid-soluble fractions of whole blood. The latter fraction contains inorganic phosphorus, phosphoric esters and undetermined compounds. Finally, the total phosphorus content of the whole blood was determined.

*From the Boston Floating Hospital, the Children's Department of the Boston Dispensary and the Pediatric Department of Tufts College Medical School, Boston.

This study was made possible by a grant from the Charlton Research Fund of Tufts College Medical School.

†Formerly Charlton Research Fellow, Tufts College Medical School.

‡Assistant professor of pediatrics, Tufts College Medical School; physician to Boston Dispensary.

The following is a brief outline of the procedure used. The details may be found elsewhere.[2, 3]

Half a given sample of blood was placed in a paraffined centrifuge tube and promptly centrifuged. The serum thus obtained was divided into four samples. Trichloracetic acid was added to one sample, which was then filtered. The protein-free filtrate was analyzed for inorganic phosphorus by adding ammonium molybdate and amino-naphthol sulfonic acid, which produces a color change to blue. After suitable dilution this was compared colorimetrically with a known standard. The other three samples of serum were digested with sulfuric acid. The last stage of the digestion was carried out with superoxal (this contains 0.0005 per cent phosphorus). The clear digest, after suitable dilution and addition of ammonium molybdate and amino-naphthol sulfonic acid, was compared colorimetrically with standard solutions. This analysis gave the total amount of phosphorus in the blood serum.

The other half of the freshly drawn venous blood was placed in a glass bottle containing a small amount of potassium oxalate. This oxalated whole blood was divided into five samples. Three of these were digested with sulfuric acid for the determination of the phosphorus content of whole blood. The fourth sample was treated with trichloracetic acid, filtered and analyzed for the acid-soluble fraction. The fifth sample was used for determination of the phosphorus of the alcohol-and-ether-soluble fraction by adding a 3:1 mixture of alcohol and ether, bringing to a boil, cooling and filtering. Portions of the filtrate were digested and prepared for the analyses.

The values recorded in Table 1 and Figure 1 represent the averages of three determinations on all blood fractions with the exception of inorganic phosphorus, wherein two determinations were made. The total of the acid-soluble and alcohol-and-ether-soluble fractions approximated the total blood phosphorus and served to check the analyses. The results were compared graphically with average values derived from controls from this clinic and with similar values derived from obtaining the average of a larger control series that included the cases of Stearns and Warweg.[4, 5] These workers made a complete study of the phosphorus of the blood in a group of 124 children.

The 33 patients from this clinic included 18 who showed clinical and laboratory evidence of rheumatic fever. (The blood sedimentation rate was considered to be the most reliable laboratory means of judging activity of the disease.) The 15 controls consisted of patients with sinusitis, pyelonephritis, skin lesions or arrested tuberculosis. Five patients from the North Reading State Sanatorium with active tuberculosis were also studied (Table 2). With these exceptions the controls were in the convalescent stages of their respective illnesses.

TABLE 1. *Phosphorus Partition in Serum and Whole Blood of Rheumatic Fever Patients and Controls.*

AGE	NO. OF CASES*	SERUM		WHOLE BLOOD			RED-BLOOD-CELL COUNT
		INORGANIC PHOSPHORUS	TOTAL PHOSPHORUS	ACID-SOLUBLE PHOSPHORUS	LIPOID PHOSPHORUS	TOTAL PHOSPHORUS	
yr.		*mg. per 100 cc.*	*mg. per 100 cc.*	*mg. per 100 cc.*	*mg. per 100 cc.*	*mg. per 100 cc.*	$\times 10^6$
5	3 R	4.9	10.8	23.3	9.9	34.0	4.1
	1 C_0	4.7	13.9	25.3	13.5	39.5	4.0
	5 C_1	5.5	15.2	28.3	12.5	41.0	
6	5 R	5.0	10.8	23.0	11.0	34.1	4.1
	2 C_0	4.8	14.2	28.3	11.9	39.8	4.8
	4 C_1	5.1	14.0	27.2	12.0	39.4	
7	1 R	4.8	12.9	24.1	8.9	33.0	4.4
	3 C_0	5.4	13.6	26.7	11.8	39.3	4.3
	3 C_1	5.3	14.1	28.2	12.3	40.7	
8	2 C_0	4.9	12.8	28.1	11.6	40.2	4.3
	5 C_1	5.1	13.7	26.2	11.7	38.1	
9	4 R	4.3	11.2	23.5	9.7	33.7	4.4
	3 C_0	5.5	12.2	28.0	12.3	40.7	4.3
	3 C_1	4.9	14.6	25.7	12.0	37.8	
10	4 R	5.2	12.7	22.1	10.2	34.6	4.6
	3 C_0	5.1	14.6	28.1	13.0	41.3	4.7
	4 C_1	5.9	15.9	28.1	12.2	40.5	
11	1 R	5.5	15.0	20.7	11.8	32.6	4.3
	3 C_0	4.7	14.2	27.0	11.4	38.7	4.4
	8 C_1	4.9	13.4	25.1	12.0	37.1	

*R — rheumatic fever patients; C_0 — Floating Hospital controls; C_1 — Stearns and Warweg controls.

In whole blood as well as in the acid fraction the highest values obtained in the rheumatic series were invariably lower than the minimum control values, including those of the North Reading group. The depletion of phosphorus was most marked in the organic fraction. The average reduction of phosphorus in the whole blood of the patients with rheumatic fever as compared with the controls was 15 per cent. There was a corresponding reduction of the available acid-soluble fraction as well as of the alcohol-and-ether-soluble fraction. There was a smaller reduction of about 10 per cent in the available serum phosphorus.

DISCUSSION

It is not impossible that the variations from normal in the rheumatic fever group are to be expected as the result of the disease itself, and have little to do with the nutritional state prior to the development of clinical and laboratory signs of rheumatic fever. However, an analysis of the problem of 65 patients in this clinic who had rheumatic fever and had clinical records antedating the proved diagnosis, as summarized in Figures 2 and 3, is strongly suggestive that the factors which tend to lower the hosts' resistance in this disease are important.

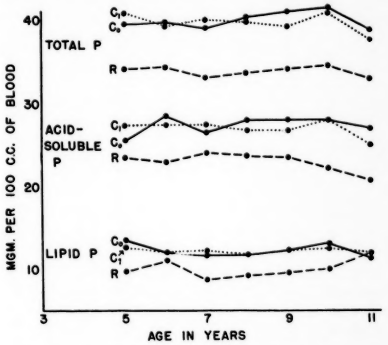


FIGURE 1. *Phosphorus Partition in Whole Blood.*

C_0 — *average of controls (20 cases).*

C_1 — *weighted average of controls, including Stearns and Warweg's patients (49 cases).*

R — *average of patients with rheumatic fever (18 cases).*

In this group comparatively large families (with an average of seven members) lived on incomes averaging about $15 a week. Consistent with the low incomes, more than 70 per cent of the patients had been inadequately nourished for several years. The nutritional histories showed that the diets were relatively rich in carbohydrates and

TABLE 2. *Phosphorus Partition in Whole Blood of Active Tuberculosis Controls.*

AGE	ACID-SOLUBLE PHOSPHORUS	LIPOID PHOSPHORUS	TOTAL PHOSPHORUS	RED-BLOOD-CELL COUNT
yr.	*mg. per 100 cc.*	*mg. per 100 cc.*	*mg. per 100 cc.*	$\times 10^6$
5	27.4	11.1	39.8	4.0
6	27.6	12.0	39.4	4.7
7	27.8	11.0	38.6	4.0
11	27.3	11.5	41.5	4.7
11	23.5	13.5	38.5	4.5
Average	26.7	11.8	39.6	4.4

starches and relatively poor in proteins, minerals and vitamins. Many of these children were ailing several months before they developed clinical signs and laboratory evidence that resulted in a diagnosis of rheumatic fever. Each patient included in our group had been followed for a varying length of time (three months to five years) before the diagnosis of rheumatic fever was entertained.

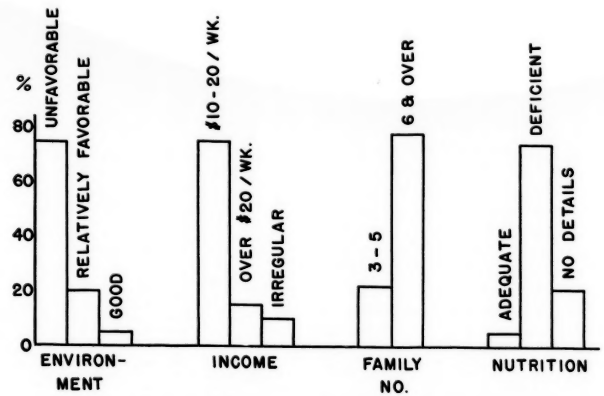


FIGURE 2. *Contributory Factors in Early Cases of Rheumatic Fever.*

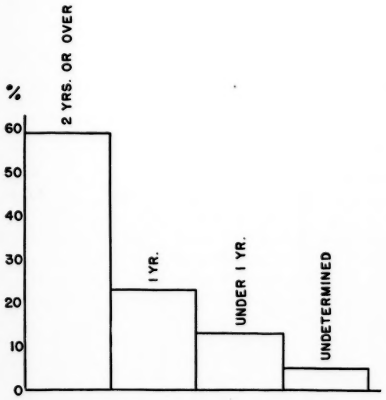


FIGURE 3. *Duration of Symptoms before Development of Clinical Signs and Laboratory Evidence Which Resulted in a Diagnosis of Rheumatic Fever.*

The most tangible evidence of undernutrition in the patients studied was a cessation of gain in weight over periods of six months or longer. Anorexia was a commonly associated complaint.

Numerous studies[6–15] indicate that rheumatic fever has a much higher incidence among the economically handicapped than among the economically independent. Those who emphasize the spread in recent years of rheumatic fever in localities said to have formerly been relatively free from the disease should take into consideration the gradual development of living conditions in these areas similar to those found in areas where the disease has been prevalent. The diets under such conditions tend gradually to become deficient in proteins, minerals and vitamins and relatively rich in the carbohydrates and starches found in less expensive foods.

Chronic fatigue was also manifested in our patients, first by lassitude and inactivity, secondly by nervous instability and wasteful overactivity. Restless, fitful sleep disturbed by night terrors was not unusual. Respiratory infections accelerated the decline in health of the patients, together with the gradual appearance of recurrent episodes of muscle, joint and visceral pain, both diffuse and localized.

This prevalence of chronic fatigue, followed later by many symptoms involving muscular tissue, raises the question of possible disturbances of metabolism of muscular tissue. Although our knowledge of the chemical reactions which occur during muscular contraction and recovery is far from complete, phosphorus compounds are considered essential for normal activity. Fiske and Subbarrow,[16] followed by Eggleton and Eggleton,[17] isolated phosphocreatine from muscle in 1927.

Chemical analyses have shown that probably 80 per cent of the creatine in resting muscle occurs as phosphocreatine. The theory has been advanced that the cleavage of phosphocreatine is the primary change that supplies the energy for normal muscular contraction. Phosphate esters including the nucleotide, adenylpyrophosphate, apparently play intermediary roles in muscular contraction and recovery.

Presumably anemia in itself should reduce the total phosphorus of whole blood. Control patients were chosen who had a reduction in erythrocytes and hemoglobin corresponding to that found in the patients who had rheumatic fever. The average hemoglobin value in both groups was about 75 per cent. The average erythrocyte count of the 20 controls was 4,500,000, and with few exceptions the count in the individual case was well over 4,000,000. The lowest control values were in a child who had lost considerable blood in the stools. His blood phosphorus values were low normal. Hematocrit readings were taken in 18 patients, including 12 with rheumatic fever. The average value for the latter was 40 per cent, as compared with 42 per cent for the controls.

Summary

The phosphorus content of the whole blood has been found to be relatively low in children with rheumatic fever, as compared with that of patients who are in a better state of nutrition, and with that of patients convalescing from acute and other chronic illnesses.

References

1. Tisdall, F. F.: Rapid colorimetric method for quantitative determination of inorganic phosphorus in small amounts of serum. *J. Biol. Chem.* **50**:329-337, 1922.
2. Fiske, C. H., and Subbarrow, Y.: The colorimetric determinations of phosphorus. *J. Biol. Chem.* **66**:375-400, 1925.
3. Stearns, G., and Warweg, E.: Studies of phosphorus of blood: partition in blood and serum, serum calcium and plasma phosphatase from birth to maturity. *J. Biol. Chem.* **102**:749-765, 1933.
4. Stearns, G., and Warweg, E.: Studies of phosphorus of the blood; phosphorus partition in blood of children with disease. *Am. J. Dis. Child.* **50**:1164-1172, 1935.
5. Warweg, E., and Stearns, G.: Studies of phosphorus of blood. II. The partition of phosphorus in blood in relation to the corpuscle volume. *J. Clin. Investigation* **13**:411-418, 1934.
6. Paul, R. R.: *The Epidemiology of Rheumatic Fever*. 117 pp. New York: American Heart Association, 1930.
7. Paul, J. R., Harrison, E. R., Salinger, R., and DeForest, G. K.: Social incidence of rheumatic heart disease: statistical study in New Haven school children. *Am. J. M. Sc.* **188**:301-309, 1934.
8. Faulkner, J. M., and White, P. D.: Incidence of rheumatic fever, chorea and rheumatic heart disease: with especial reference to its occurrence in families. *J. A. M. A.* **83**:425, 1924.
9. Fishberg, A. M.: *Heart Failure*. 788 pp. Philadelphia: Lea & Febiger, 1937.
10. Swift, H. F.: Rheumatic fever. Cecil's *Text Book of Medicine*. Fourth edition. 1614 pp. Philadelphia and London: W. B. Saunders Co., 1937. Pp. 474-490.
11. Miller, R.: Report on environmental and other predisposing causes of rheumatic infections. *Brit. M. J.* **2** (supp.):5-10, 1926.
12. Glover, J. A.: Milroy lectures on incidence of rheumatic fever diseases: incidence of acute rheumatism. *Lancet* **1**:499-505, 1930. Milroy lectures on incidence of rheumatic diseases: rheumatism in industry. *Ibid.* **1**:607-612, 1930. Milroy lectures on incidence of rheumatic diseases: incidence of chronic arthritis. *Ibid.* **1**:733-738, 1930.
13. Acute rheumatism in children in its relation to heart disease. *Reports on Public Health and Medical Subjects from the Ministry of Health*. No. 44. 99 pp. London: His Majesty's Stationery Office, 1927. Pp. 25-50.
14. Nobel, E.: Statistik und Prophylaxe der Klappenfehler. *Wien. klin. Wchnschr.* **41**:125-127, 1928.
15. Maddox, K.: Metropolitan and rural incidence and distribution of acute rheumatism and rheumatic heart disease in New South Wales. *M. J. Australia* **1**:394-399, 425-432, 464-467 and 499-504, 1937.
16. Fiske, C. H., and Subbarow, Y.: The nature of the "inorganic phosphate" in voluntary muscle. *Science* **65**:401, 1927.
17. Eggleton, P., and Eggleton, G. P.: The physiological significance of "phosphagen." *J. Physiol.* **63**:155-161, 1927.

END RESULTS OF USE OF LARGE DOSES OF AMPHETAMINE SULFATE OVER PROLONGED PERIODS*

Wilfred Bloomberg, M.D.†

BOSTON

AMPHETAMINE (Benzedrine) sulfate was introduced into therapy in December, 1935.[1] Since our report of its use in narcolepsy, many studies have been carried out, and numerous reports have appeared in the literature which deal with the physiology, clinical uses and toxicology of this interesting drug. The effects of amphetamine on blood pressure, mood, intelligence and gastrointestinal functions have been exhaustively studied. The great majority of reports, however, deal with the effect of single doses, or of small doses over a comparatively short period of time. Ulrich[2] in October, 1937, reported follow-up studies on some of his narcoleptic patients after months of treatment. However, the effect on the bodily physiology of extremely large doses over comparatively long periods of time has not so far been reported. It seemed worth while, therefore, to present the results of studies of 3 patients with narcolepsy who have been taking at least 70 mg. of amphetamine sulfate every day, for two years and eight months in 2 cases, and for one year and eight months in 1. Two of the patients were cases in our original series, and the third started treatment some time after the original group.

*From the Department of Neurology, Harvard Medical School, and the Neurological Unit, Boston City Hospital.

†Instructor in neurology, Harvard Medical School; assistant visiting neurologist, Boston City Hospital.

Method

The three patients all suffered from narcolepsy and cataplexy. In 2 cases these symptoms developed after an attack of encephalitis lethargica, and

in 1 of these the narcolepsy was accompanied by postencephalitic parkinsonism; in the third case the narcolepsy was of the so-called "idiopathic" type. Two patients were women, aged twenty-seven and twenty-three, and 1 was a man, aged sixty-two. In 2 cases fairly complete laboratory studies of the pre-treatment period were available; in the third these were unfortunately not at hand.

In the follow-up studies, each of the 3 patients was admitted to the hospital for a period of observation and study of at least three days. In order to determine whether there were any toxic effects on the kidneys, urine examinations, Mosenthal tests and phenolsulfonephthalein excretion tests were carried out, and the blood nonprotein nitrogen was determined. For the effect on the liver, icteric index and Takata-Ara tests were done. The effect on the cardiovascular system was studied by four-hourly blood-pressure readings during the entire stay in the hospital, and by seven-foot heart x-ray plates in 2 cases. In 1 case in which a pre-treatment electrocardiogram had been taken, this was repeated.

The endocrine system was studied by determination of the basal metabolic rate and the blood sugar, and by charting the pulse rate, as well as by inquiring into a history of change in weight. The blood was studied by counts and the examination of smears. A careful history was taken, and general physical and neurological examinations were made. In taking the history, special emphasis was placed on eliciting evidence of abnormal cutaneous manifestations and of gastrointestinal symptoms.

Not every one of the tests was carried out on each patient, but a sufficient number of laboratory investigations was made in each case to uncover any abnormality of function of any system.

TABLE 1. *Comparison of Laboratory Findings Before and After Prolonged Use of Large Doses of Amphetamine (Benzedrine) Sulfate in Three Patients with Narcolepsy.*

FACTS AND TESTS	CASE 1		CASE 2		CASE 3	
Sex	Female		Female		Male	
Age (years)	27		23		62	
Diagnosis	Postencephalitic narcolepsy; cataplexy		Narcolepsy; cataplexy; migraine (?)		Postencephalitic parkinsonism; narcolepsy; cataplexy; obstructive prostate	
Dose of amphetamine	110–120 mg. daily (1 yr.); 70–80 mg. daily (1 yr. 8 mo.)		80 mg. daily (2 yr. 8 mo.)		70–100 mg. daily (1 yr. 8 mo.)	
	Before	*After*	*Before*	*After*	*Before*	*After*
Hemoglobin (per cent)	80, 82	78	95	96	—	77
Red-cell count (millions)	4.1, 5.3	4.1	4.8	4.8	—	4.0
Blood smear	Normal	Normal	Normal	Normal	—	Normal
White-cell count (thousands)	9.2	6.1	7.6	8.6	—	6.9
Differential white-cell count	Normal	Normal	Normal	Normal	—	Normal
Urine	Occasional albumin	Negative	Negative	Negative	—	Trace of albumin
Phenolsulfonephthalein test (per cent)	—	35	—	50	—	55
Nonprotein nitrogen (mg. per 100 cc.)	34	24	—	28	—	26
Blood sugar (mg. per 100 cc.)	87	87	—	89	—	101
Creatinine (mg. per 100 cc.)	—	1.2	—	—	—	1.5
Blood pressure (mm. of Hg.)	110/80	105/70 to 90/50	120/80	110/65 to 80/50	—	120/75
Basal metabolic rate (per cent)	−25, rising to −5 on thyroid (7½ gr. daily)	−17, −23	—	−6	—	−5
Electrocardiogram	Normal rhythm; T_2=1.5 mm.	Low T waves (? significant)	—	—	—	—
Mosenthal test (range)	—	1.018 to 1.024	—	1.012 to 1.023	—	1.020 to 1.022
Takata-Ara test	—	Negative	—	Negative	—	Negative
Icteric index (per cent)	—	5	—	—	—	5
Seven-foot x-ray plate	—	Normal	—	—	—	Normal

COMMENT

Reference to Table 1 will show that in spite of the massive doses of amphetamine, continued over a comparatively long period, no significant abnormality was found in any of the tests. The temperature, pulse and respiratory rate were normal throughout. There was no increase in the basal metabolic rate and no rise in blood pressure. There was no evidence of damage to the kidneys or liver. The blood and certain of its constituents showed no deviation from the normal.

General physical and neurological examinations were entirely negative in all cases. None of the patients had suffered skin or gastrointestinal disturbances. They were all keeping awake on amphetamine sulfate, and were able to carry on their work. Cataplexy was almost entirely relieved in each. None of them had had to increase

the dose of amphetamine after the adjustment period of the first few weeks, and one (Case 1) had actually found that she could lower it. None of them felt any craving for the drug or was unwilling to stop taking it during the study period. The usual comment was, "Now that I'm in bed and have nothing to do and don't mind sleeping, I don't mind not taking the pills."

My recent experience with amphetamine sulfate has included the treatment of a great number of alcoholic patients. These patients do not, of course, take such large doses, but some of them take as much as 50 mg. per day, and in no case in my series has there been any significant difficulty attributable to the drug for more than a day or so. No patient in my experience has had to give up his medication because of untoward side effects. Nor have I observed any evidence, in either the narcoleptic or the alcoholic group, of addiction, habit formation or increase in tolerance after the first two or three weeks of treatment. Incidentally, though other writers have warned against the use of amphetamine sulfate outside the hospital, all these patients have been ambulatory, and no difficulties have been encountered because of this fact. One alcoholic patient did, indeed, because of his state of intoxication at the first interview, misunderstand his instructions. He thought the tablets were a sedative, and so took more and more as he became more excited. He had finally consumed 150 mg. in about fourteen hours, but other than a sleepless night and a jumpy irritability, lasting about thirty-six hours, he suffered no ill effects.

Summary and Conclusions

Three patients with narcolepsy who had been taking 70 mg. or more of amphetamine sulfate daily for two years and eight months in 2 cases, and for one year and eight months in 1 case, were studied.

No significant deviation from normal, as a result of this large dosage, was found in any case by any laboratory or clinical study.

No evidence of addiction or habit formation was found.

189 Bay State Road.

References

1. Prinzmetal, M., and Bloomberg, W.: The use of benzedrine for the treatment of narcolepsy. *J. A. M. A.* **105**:2051-2054, 1935.
2. Ulrich, H.: Narcolepsy and its treatment with benzedrine sulfate. *New Eng. J. Med.* **217**:696-701, 1937.

PREVENTION AND MANAGEMENT OF PAIN FOLLOWING CHOLECYSTECTOMY*

John M. McGowan, M.D.,† and Francis F. Henderson, M.D.‡

BOSTON

A GREAT deal has been said and written in recent years concerning unsatisfactory results following surgical removal of the gall bladder. After being exposed to a procedure of such magnitude the patient expects to enjoy good health and freedom from symptoms. Unfortunately, in many cases the pain and discomfort return, and are as severe after operation as they were before it.

We have divided our cases into two groups: those in which the pain was produced from the beginning, by disturbances outside the biliary system, and those in which the symptoms were caused primarily by disease in the biliary tract and in which cholecystectomy was a necessary procedure. In the first group, obviously no relief can result from removal of the gall bladder, even though it might incidentally have been diseased. It is with the second group of cases that this paper is concerned.

In order to prevent recurrence of biliary colic after operation, it is necessary for the surgeon to have a complete understanding of the physiologic disturbance involved. McGowan, Butsch and Walters[1] early in 1936 demonstrated that biliary pain could be produced by increased pressure within the bile ducts. This pressure is often due to obstruction in the common duct, which may be the result of an unsuspected stone, swelling in the head of the pancreas, a stricture of the common duct or spasm of the muscle at the lower end of the common duct. It was found that morphine produced this spasm, and in a number of cases the resulting back pressure in the bile ducts produced biliary colic. The drug when given in large doses relieved the pain by acting on the cortical centers, but it augmented and prolonged the spasm. In this way it exposed the bile ducts to periods of distention lasting from eight to twelve hours.

When the bile ducts are dilated, high tensions are developed within them as a result of increased pressure. These tensions are poorly withstood by the thin-walled ducts and pain results. Morphine relieves the pain, but appears to shorten the inter-

*From the Fourth Surgical Research Laboratory, Boston City Hospital.
†Assistant in surgery, Boston City Hospital.
‡Chief of the Fourth Surgical Service, Boston City Hospital.

val between subsequent attacks. Inhalation of amyl nitrite or the sublingual administration of glyceryl trinitrate (nitroglycerin) relaxes the spasm, reduces the pressure and relieves the pain (Fig. 1). Nitroglycerin, in doses of one or two

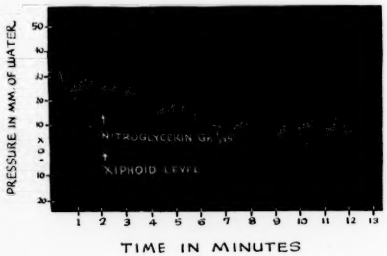


FIGURE 1.

Pressure-tracing of the common duct showing only a slight increase in the resting pressure. Reduction of the pressure by means of glyceryl trinitrate indicates the presence of duodenal spasm. Roentgenograms of this case are illustrated in Figure 3.

tablets, each containing 1/250 gr., has been found to be of consistent potency. In a recent publication[2] it was shown that the sphincter mechanism of the common duct is the muscle of the duodenal wall. Since a physiologic sphincter functioning independently of the duodenal wall has never been demonstrated, it seems proper to use the term "duodenal spasm" where the term "spasm of the sphincter of Oddi" is generally employed. The physiological principles just outlined should be kept in the foreground of the surgeon's mind if he is to prevent biliary complications after cholecystectomy. The first step in this direction is the proper use of T-tube drainage of the common duct.

T-TUBE DRAINAGE

T-tube drainage decompresses the ducts of the biliary tree. This allows the ducts in many cases to return to normal size and the inflammation in them to subside. The ducts are then able to withstand higher pressures without producing pain. An indwelling T tube in the common duct allows future detailed study of the patency of the papilla of Vater by a series of pressure studies. Also, it permits roentgenographic studies for the detection of missed common-duct stones.

At the time of operation the common duct may be opened in most cases before removal of the gall bladder. The clamped cystic duct may be used as a retractor to steady the common duct. Indications for opening the duct are a history of jaundice, the presence of a palpable stone in the duct, a markedly dilated duct and inflammation in the head of the pancreas. Lahey[3] estimated that 40 per cent of all cholecystectomies should be accompanied by exploration of the common bile and hepatic ducts. In each case a T tube should be left in the common duct for drainage.

During exploration of the common duct the patency of the papilla of Vater should be determined by passing graduated, soft-woven catheters down through the common duct into the duodenum. Zollinger[4] has stated that No. 10 Fr. is the size of the average lumen of the papilla of Vater in the human subject. Overdilation of the papilla of Vater may lead to scar formation, and to narrowing of the lumen to less than its original size.

The T tube is best brought to the surface in the center of the wound. It should be placed so that there is an excess of tube between the common duct and the abdominal wall. This allows a certain play on the tube by the movements of the abdominal wall in respiration. If this precaution is not taken the gradual pull on the tube will kink the common duct. The tube should be fastened to the skin with a silk suture. Care must be taken not to constrict the tube.

In the aftercare of these patients it is very important to have a proper method for collecting the bile. Nothing must be attached to the tube which might pull on it. A suitable apparatus consists of an 8-ounce flat medicine bottle with a baby's nipple attached. The bottle is fastened to the binder by means of adhesive tape. The end of the T tube should be pushed through a hole in the nipple. This hole must be sufficiently large to allow the escape of air. If not, pressure within will stop drainage. After the patient becomes ambulatory, a small hot-water bottle with a metal tube inserted through the stopper makes a convenient bag for collecting bile.

Two weeks after operation, tests are carried out in order to determine the probable duration of T-tube drainage. These consist in determinations of the resting intrabiliary pressure, and of the perfusion pain level and roentgenographic studies of the biliary tract.

RESTING INTRABILIARY PRESSURE

The resting intrabiliary pressure is measured by a special apparatus, described elsewhere.[1] This apparatus is built around an ordinary Y-shaped glass tube. The stem of the Y is attached by means of a rubber tube to a bottle of intravenous saline solution. To each limb of the Y tube is attached a rubber tube, one of which is to be connected to the T tube in the patient, the other to

an upright spinal manometer. The tubing is filled with saline solution from the reservoir bottle before it is connected to the patient. The zero level of the manometer should be placed at the level of the xiphoid process of the sternum. The resting fluid level in the manometer is ordinarily at about this point. If the resting fluid level is considerably above the base line, say 30 to 100 mm., one should suspect some partial obstruction in the lower end of the common duct. This may be due

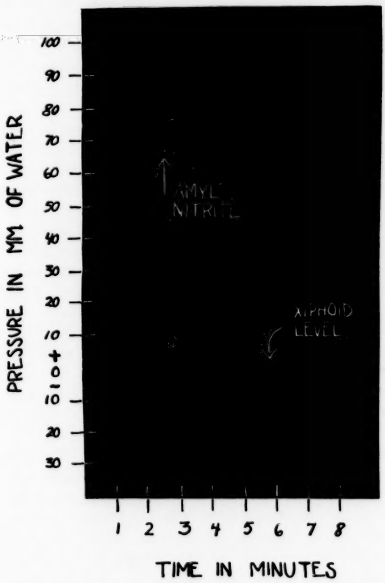


FIGURE 2.

Pressure-tracing of the common duct illustrating a moderate increase in the resting pressure above the normal. Amyl nitrite produced only partial reduction in the pressure. This shows that the pressure is due partially to spasm but chiefly to a more permanent cause. Roentgenograms of this case are illustrated in Figure 4.

to pressure from inflammation in the head of the pancreas, spasm of the musculature of the duodenal wall, a missed stone in the common duct or edema of the duodenal mucosa at the ampulla of Vater.

Five deep inhalations of amyl nitrite will aid in determining the nature of the obstruction. If this medication reduces the pressure to normal, the obstruction is due entirely to spasm. If it fails to reduce it, the obstruction is of a more permanent nature. If it reduces it incompletely, obstruction is due partially to spasm and partially to some more permanent cause (Fig. 2).

Perfusion Pain Level

Perfusion of the common duct is done in order to determine the amount of pressure that it will withstand without producing discomfort. The lowest pressure level in the common duct at which the patient complains of pain is referred to as the "pain level." Some patients experience pain when the biliary tree is exposed to relatively low perfusion pressures, at times not over 70 mm. of water. In other cases pressures of 500 mm. or more may be tolerated without discomfort. There are two reasons for this difference. In the first place, if the bile ducts are dilated, high tension is developed by relatively low pressures. Secondly, if the ducts are inflamed from the presence of infection, they withstand pressure rather badly. The bile passages should be able to resist pressures of 300 mm. of water without producing pain. This is usually the maximum secretion pressure of the liver. If pressures below 300 mm. of water produce pain or discomfort, the patient may expect to have recurrence of distress after removal of the T tube. On the other hand, if the bile ducts are decompressed for a sufficiently long time by T-tube drainage, dilatation and infection will improve and the bile ducts can resist relatively high pressure. Under these circumstances, if the patient subsequently has duodenal spasm for a few hours the resulting back pressure in the bile ducts will not produce pain.

To determine the pain level the pressure apparatus is connected to the patient as described. The reservoir bottle is lowered until its fluid level is the same as that of the zero level of the manometer. The clamp is taken off the rubber tube from the reservoir bottle, which is slowly elevated until the patient experiences discomfort. The fluid level in the manometer is then read. This reading is the pain level. The tube from the reservoir bottle is reclamped. The fluid in the manometer then falls in two to five minutes to a level equal to the resting intrabiliary pressure. The perfusion pain level should be over 300 mm. of water; the resting intrabiliary pressure should be less than 30 mm. of water.

Roentgenographic Studies of the Biliary Tract

For roentgenographic studies the patient is placed flat on his back on the x-ray table and all the preparations to take the pictures are made;

10 cc. of Diodrast* in a syringe is injected slowly into the T tube. A roentgenogram is taken immediately. The tube is clamped, and a second roentgenogram is taken ten minutes later. Study of the films will show whether any obstruction to the flow of bile into the duodenum exists. Obstruction is indicated by extreme dilatation of the main ducts and small branches of the biliary tree, and by failure of the ducts to empty after a ten-minute interval. Spasm of the duodenal musculature is indicated on the x-ray film by a narrowing of the lower end of the common duct to a sharp pencil point (6 in Fig. 3*A* and *B*); this is not present in pictures taken one minute after five deep inhalations of amyl nitrite. Duodenal spasm may be indicated by roentgenographic study of the duodenum under a special method previously described.[2]

*Supplied through the courtesy of the Winthrop Chemical Company, New York City.

Stricture of the mucous membrane of the ampulla of Vater is indicated in the lower end of the common duct by the presence of a blunt, rounded termination (below 6 in Fig. 4*B*).

In these cases the opaque medium frequently outlines the proximal portion of the pancreatic duct. When the medium is injected, epigastric pain is often experienced. This pain is undoubtedly due to pressure within the pancreatic duct. It is complained of occasionally by sufferers from biliary-tract disease, and tends to complicate the differential diagnosis between cholecystitis and peptic ulcer.

Unsuspected stones in the common duct can frequently be made to pass by applying the following procedure. Attach the pressure apparatus to the T tube and slowly raise the perfusion pressure to the level of toleration or to 500 mm. of water. Then have the patient take five deep inhalations

A B

FIGURE 3.

A. *This film shows the common duct under resting conditions. The numbering in this illustration and in Figure 4 is as follows:* 1, *common duct;* 2, *point at which the bile enters the duodenal lumen;* 3, *contrast medium in the duodenum;* 4, *hepatic ducts and the finer radicles in the biliary tree;* 5, *pancreatic duct;* 6, *point at which the common duct begins to penetrate the musculature of the duodenal wall;* 7, *T-tube;* 8, *cystic duct;* 9, *Sawyer tube passed through the nose into the duodenum. Definite narrowing of the common duct can be seen at* 6. *This is due to spasm. The portion of the duct between* 6 *and* 2 *is that part which tunnels the duodenal wall, the intramural portion.*

B. *This film of the same case was taken ten minutes after the subcutaneous injection of ⅙ gr. of morphine. The spasm at* 6 *has greatly increased, producing almost complete obstruction. The common duct is much more distended as a result of back pressure.*

of amyl nitrite. Frequently the sudden release of spasm will allow the pressure of the saline solution to force the stone into the duodenum. This procedure may be repeated as often as desired until roentgenograms show disappearance of the stone.[5]

Later Care

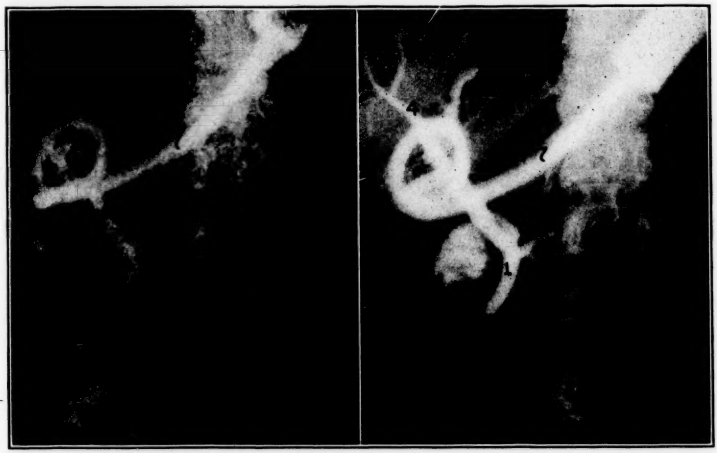
About two weeks following operation the patient is instructed to begin clamping off the T tube. Starting with a half hour twice daily, the time is increased until the tube is clamped off all the time. If the patient experiences distention or pain during the clamping he is instructed to place one to two 1/250 gr. tablets of glyceryl trinitrate under the tongue. If he does not obtain relief of pain in five minutes, the tube is unclamped and allowed to drain. The tube may be removed in three weeks or left in for six months, as indicated.

If the patient can keep the tube clamped off continuously for three weeks and be free of pain, it is safe to remove it, provided the pain level is above 300 mm. of water, the resting pressure level is below 30 mm. of water, and the roentgenograms show absence of stones and free emptying of the T tube. The patient is instructed to take glyceryl trinitrate as required for distention or pain.

In the case of postoperative patients in which cholecystectomy was performed without T-tube drainage, we prescribe glyceryl trinitrate for nausea, distention or biliary colic. During the first few days after operation we use dilaudid freely for the control of pain. Any untoward symptoms caused by this drug may be neutralized by glyceryl trinitrate.

Medical Treatment of Biliary-Tract Disease

The patient who returns several months or years after cholecystectomy complaining of repeated attacks of typical biliary colic presents a problem to the surgeon. A diagnosis of biliary dyskinesia can usually be made by the characteristic location of the pain in the right subcostal region, extending around into the right scapular region. At times the pain reaches the tip of the shoulder, or it may extend down into the lumbar region and direct one's attention to the kidney. A test dose of morphine, 1/6 gr. given subcutaneously, will usually bring on a characteristic attack of pain in five minutes to one-half hour. An induced attack is readily relieved by inhalation of amyl nitrite or by sublingual administration of one or two 1/250 gr. tablets of glyceryl trinitrate.



A B

Figure 4.

A. *This is a choledochogram taken under resting conditions, showing moderate spasm at 6 and stricture of the ampulla of Vater at 2.*

B. *Following inhalation of amyl nitrite the spasm has disappeared at 6, the opaque medium has been allowed to flow freely into the ampulla of Vater and, finding obstruction at the duodenal mucosa, has regurgitated into the pancreatic duct. The patient experienced severe midepigastric pain at this time.*

In such cases we prescribe one or two 1/250 gr. tablets of glyceryl trinitrate every three hours for three days, and one three times daily after meals and at bedtime for three weeks. This procedure keeps the pressure in the biliary system at a low level and promotes a free flow of bile into the duodenum. The patient is allowed a general mixed diet. Cooked fats and fried foods are eliminated. The patient is encouraged to take cream and eggs freely. This course of treatments produces permanent relief of symptoms in most cases. If this treatment fails, a second operation must be considered in order to explore the common bile duct for missed stones.

We have used similar treatment in cases of cholecystitis with gall bladders that fill and empty freely and do not contain stones. We have had 6 such cases with symptoms of cholecystitis for two to fifteen years, the patients varying in ages from twenty-two to sixty-five years. After a course of treatment as outlined they have been entirely symptom-free for periods up to one and a half years. We have found this treatment useful for 4 patients with stone-filled gall bladders, in whom a surgical procedure carried an increased risk because of advanced age, hypertension or coronary disease. All have been rendered symptom-free by a course of glyceryl trinitrate. They frequently report prompt relief of individual attacks after single doses. Two of these patients were moderately jaundiced when treatment was started. Icterus disappeared in a few days and has not returned. One patient has been symptom-free for one year, and the other for four months. One of the others has since had an attack of cerebral hemiplegia, proving the advisability of deferring operation.

We do not advise this treatment in cases of cholelithiasis except as a temporary procedure or when operation is contraindicated. We believe at present that a stone-filled gall bladder or one which is not functioning should certainly be removed if the patient's condition permits.

Summary

Biliary colic following cholecystectomy is due to obstruction of the common duct, preventing the flow of bile into the duodenum. Obstruction of the common duct may be due to stone, stricture, edema or spasm. The back pressure results in pain. Common-duct pressure of 70 mm. of water produces pain in some individuals, while 500 mm. may be withstood by others with impunity. Prolonged T-tube drainage allows the common duct to resist greater pressures. Glyceryl trinitrate relaxes duodenal spasm and tends to lower the resting intrabiliary pressure. Methods of studying the patency of the papilla of Vater and the condition of the bile ducts are described.

Biliary dyskinesia and many symptoms of cholecystitis are relieved by a course of treatment consisting of the daily use of glyceryl trinitrate to relax duodenal spasm.

References

1. McGowan, J. M.; Butsch, W. L., and Walters, W.: Pressure in the common bile duct of man: its relation to pain following cholecystectomy. *J. A. M. A.* 106:2227-2230, 1936.
2. McGowan, J. M.; Knepper, P. A.; Walters, W., and Snell, A. M.: The relation of spasm of the second portion of the duodenum to biliary colic. *Surg., Gynec. & Obst.* 66:979-987, 1938.
3. Lahey, F. H.: Common and hepatic duct stones. *Am. J. Surg.* 40:209-216, 1938.
4. Zollinger, R.; Branch, C. D., and Bailey, O. T.: Instrumental dilatation of the papilla of Vater: experimental and clinical observations. *Surg., Gynec. & Obst.* 66:100-104, 1938.
5. Walters, W., and Wesson, H. R.: Fragmentation and expulsion of a common duct stone into the duodenum by using ether and amyl nitrite. *Surg., Gynec. & Obst.* 65:695-697, 1937.

THE IMPORTANCE OF INVESTIGATING THE CAUSE OF RENAL PAIN

HOWARD G. NICHOLS, M.D.*

HAVERHILL, MASSACHUSETTS

"ITERATION and reiteration" was one of Dr. Oliver Wendell Holmes's favorite medical mottoes, for he believed that medical knowledge and its application were greatly enhanced thereby. The substance of this paper has been iterated extensively and the principles involved are elucidated in many textbooks. Yet the very fact that the cases herein reviewed exist is evidence of the justification for this bit of reiteration.

Local color makes any scene more impressive, and so, too, the presence of blood in the urine and the consequent need for ascertaining its cause appear to be more impressive, to laymen and physicians alike, than does the occurrence of pain along the urinary tract. Gross hematuria is something that the patient can see; though it may cease, its occurrence implies that something is wrong, and as a result a cause for it is much more apt to be sought. On the other hand, when pain is the only presenting symptom there is nothing to see, and, if the attack promptly subsides, interest in the condition is often dissipated — usually in proportion to the rapidity with which the pain subsides; again, the patient decides to wait for another attack before attempting to ascertain its cause. As a consequence, adequate investigation is often not initiated until appreciable or, in fact, irreparable damage has occurred.

In three of the following cases which ultimately required nephrectomy, conservative measures instituted soon after symptoms first occurred would very likely have restored normal function and thereby preserved the integrity of the organ, while in the fourth case, though it would have been necessary to sacrifice the kidney, it would have been less discouraging to do a nephrectomy for potential than for actual cancer.

CASE 1. L. M., a 16-year-old girl, presented a 7-year history of left lumbar pain, occurring two to three times a week and lasting from 1 hour to 2 days at a time. The pain was usually a dull aching sensation, occasionally becoming sharp and radiating to the left groin. No history of dysuria, frequency, nocturia or hematuria was obtained. Six years previously, however, the patient was hospitalized because of fever and pyuria. No renal study other than routine urine examination was made at that time. A few weeks prior to admission to the hospital, she had been discharged from a tuberculosis sanatorium with a diagnosis of "childhood-type pulmonary tuberculosis, arrested," and had been told that she should have her kidneys investigated to ascertain the cause of recurrent pain.

On admission the patient complained of a moderate amount of dull lumbar pain. Physical examination showed nothing remarkable except considerable tenderness over the left costovertebral area. The blood pressure was normal. A catheterized specimen of urine had a specific gravity of 1.020 and contained no albumin or sugar; the sediment contained occasional white blood cells and rare red cells.

Intravenous pyelography revealed no excretion from the left kidney. The right kidney and ureter appeared normal. Cystoscopic examination showed a normal-appearing bladder. A No. 6 Fr. ureteral catheter was readily passed up the left ureter. Thirty cubic centimeters of clear residual urine was obtained from the kidney pelvis, and the urine removed from this kidney showed a normal sediment and no growth on culture. Guinea-pig inoculation was negative for tuberculosis. Retrograde pyelography revealed a very small left kidney with marked dilatation and blunting of all the calyces, together with a definite ureteropelvic stricture (Fig. 1).

FIGURE 1.

Note the ureteropelvic stricture and the dilatation of the calyces.

*Chief of Urological Service, Haverhill Municipal Hospital; assistant surgeon, Urological Department, Boston Dispensary.

A left nephrectomy was performed, an atrophic hydronephrotic kidney being removed without difficulty. The ureter appeared normal except at the ureteropelvic junction, where there was definite narrowing and evidence of chronic periureteral inflammation and fibrosis. No aberrant vessels were discovered. The pathological report was as follows:

> The specimen consists of a kidney measuring 6 by 3 cm. The cortex is extremely rough and granular, while the cut surface shows a replacement of the normal parts by numerous large dilatations of the calyces. Inflammatory changes are apparent in the walls. The function in this kidney had apparently ceased. The tubules are atrophic, and there is a tremendous infiltration of mononuclear leukocytes, lymphocytes, plasma cells, neutrophils and eosinophils. A great deal of interstitial hemorrhage has taken place. Diagnosis: Chronic pyelonephritis and hydronephrosis.

222
40

This is the history of a 16-year-old girl with a seven-year story of left lumbar pain, with one hospital admission because of pyuria, who was not studied urologically until seven years after the onset of symptoms. There was a combination of impaired development and kidney destruction, both of which might well have been obviated by judicious dilatation of the ureter and treatment of the infection when the signals of distress were first evident.

Case 2. A. F., a 34-year-old, married woman, 5½ years previous to admission, when 3 months pregnant, developed an attack of pain in the right kidney region accompanied by pyuria. She was hospitalized for 5 days, during which time an unsuccessful attempt was made to perform pelvic lavage. One and a half months later, and again 2 weeks postpartum, she suffered recurrences. These attacks were accompanied by chills, fever and nausea. Since then she had had about one attack of pain per year, each attack lasting 3 or 4 days. Between attacks she had been symptom-free. No x-ray photographs had ever been taken. The last episode began 3 days before admission, with a dull pain in the right costovertebral angle, radiating to the right upper quadrant of the abdomen. There was slight dysuria, and the urine had become reddish.

Physical examination revealed no abnormalities. The urine showed a large amount of albumin but no sugar. The sediment contained many red and white blood cells.

Cystoscopy revealed a rather prominent right ureteral eminence with an orifice barely large enough to admit a No. 6 Fr. catheter. Forty cubic centimeters of milky residual urine was obtained from the right kidney pelvis and 3 cc. of clear urine from the left kidney pelvis. A phenolsulfonephthalein functional test showed no excretion on the right side. A culture of the urine from the right kidney was reported as positive for *Bacillus proteus,* and one of that from the left as negative. Retrograde pyelography showed right nephrolithiasis, marked hydronephrosis and hydroureter involving the entire ureter down to the ureterovesical junction (Fig. 2).

A right nephrectomy and partial ureterectomy was performed. Only a moderate amount of perirenal reaction was encountered. In view of the proteus infection and the extensive involvement of the ureter, a nephroureterectomy had been planned, but the condition of the patient did not warrant so extensive a procedure. Consequently a complete ureterectomy was postponed. The pathological report was as follows:

> The specimen consists of a kidney and attached ureter. The latter is thick-walled and tremendously dilated. The kidney is increased in size. The surface shows many fetal lobulations. The cut surface shows tremendous dilatation of the pelvis and calyces, which has converted the organ into a large, thin-walled, cyst-like structure. The wall of the pelvis is thick, granular and congested. The organ contains one large stone

Figure 2.
Note the extensive hydronephrosis and hydroureter.

> which measures 2.0 by 1.5 by 1.5 cm., and three smaller stones averaging 5 mm. in diameter. The kidney tissue weighs only 100 gm. Sections throughout the pelvis show a tremendous chronic inflammatory reaction. The glomeruli are engorged with blood, and the surrounding tubules exhibit granular degeneration. Throughout the medullary portion chronic inflammatory changes are visible. Diagnosis: Nephrolithiasis, hydronephrosis and chronic ascending interstitial nephritis.

Two and a half weeks postoperatively, specimens of bladder urine and fluid from the right ureter, while showing numerous while cells, were negative on culture. Accordingly ureterectomy was postponed in order to see whether the pyuria could not be controlled by other measures. Three months later the patient was symptom-

free, and the urine showed only occasional white cells. Apparently ureterectomy will not be necessary.

This case had a five-and-a-half-year history of renal pain and chronic infection. Adequate treatment of the infection and dilatation of the ureter early in the course of the disease might well have averted this sequence of events.

CASE 3. H. N., a 41-year-old, married woman, 8 years previous to admission began having attacks of sharp pain over the left lower ribs in the axillary line. The pain did not radiate to the flank or costovertebral angle, nor was it

FIGURE 3.

Note the large kidney with massive dilatation of the calyces.

influenced by respiratory movements. It was severe enough at times to cause perspiration. The attacks lasted half a day and recurred every 3 months to 1 year until 4 years previously, since when there had been only minor episodes of pain in this area. There were three episodes of transitory gross hematuria following attacks of pain. No history of dysuria, frequency or nocturia was obtained. The patient was referred to the hospital for study because of pyuria and a systolic blood pressure of 160.

Examination, except for hypertension, was not remarkable. The urine showed a slight trace of albumin and a sediment containing innumerable white blood cells.

Cystoscopy showed a normal bladder mucosa. The ureteral orifices and bladder neck appeared normal. A No. 6 Fr. catheter was passed to the right kidney pelvis. A catheter could be passed only about halfway to the left kidney pelvis. No residual urine was aspirated from either side. The urine from the right kidney pelvis was normal; that from the left ureter showed many white blood cells. A phenolsulfonephthalein test was normal on the right side, and zero on the left. Culture of the urine from the left ureter was negative; that of the bladder urine showed streptococci. Retrograde pyelography revealed a sharp angulation of the left ureter at the level of the fourth lumbar vertebra, beyond which neither catheter nor Diodrast solution passed. What appeared to be a greatly enlarged kidney shadow extended from the iliac crest to above the 11th rib. Intravenous pyelography showed faint, widely separated splotches of media characteristic of extensive hydronephrosis (Fig. 3).

Nephrectomy was performed, a large, hydronephrotic kidney being removed. Immediately below a greatly dilated pelvis there was an S-shaped kinking of the ureter, which was maintained by adhesive bands, thereby forming a marked obstruction to the ureteral flow. This obstruction was located at about the level of the 4th lumbar vertebra. The pathological report was as follows:

> The specimen consists of a kidney which has been very largely converted into a series of cyst-like pockets, all of which are filled with a blood-tinged fluid. The renal parenchyma has thereby been reduced to a small rim of tissue except at the lower pole, where an intact portion measuring 2 by 2 cm. remains. The thin rim of the cortex shows atrophy of the glomeruli and tubules, and heavy round-cell infiltration. Diagnosis: Hydronephrosis, with chronic inflammation.

This case presents an eight-year history of somewhat atypical renal pain, with three attacks of gross hematuria (not even hematuria induced her to seek adequate study) and eventual destruction of the kidney due to ureteral obstruction and infection. A nephropexy with a lysis of adhesions might have overcome the obstruction if undertaken early enough. However, only the end result was observed, and the low position of the kidney may well have been due simply to its enlargement. As a result, it is difficult to say what operative measures would have been necessary, but certainly they would have been no more radical than those that were ultimately adopted. This patient was originally on the medical service for study of her hypertension. The presence of pyuria and the history of the case suggested the possibility of hypertension due to unilateral renal disease and hypertension. However, the blood pressure became normal soon after admission and before operation. Following discharge from the hospital the hypertension recurred.

CASE 4. H. H., a 45-year-old man, complained of painless hematuria of 1 week's duration. He had no other complaints, aside from a feeling of lassitude. For the last 31 years he had had numerous attacks of colicky pain in the left costovertebral region and left flank, unaccompanied by chills, fever or symptoms of bladder irritation. These attacks were severe enough to require repeated injections of morphine. So far as he knew, his urine had never shown anything abnormal. No urological studies had ever been made.

Physical examination gave essentially negative results.

Cystoscopy revealed a normal bladder, with grossly bloody fluid issuing from the left ureteral orifice. Retro-

grade pyelography showed kinking of the ureter and distortion of the renal pelvis by what appeared to be a tumor mass. Hydronephrosis was also present (Fig. 4).

At operation a slightly enlarged kidney was found.

FIGURE 4.

Note the deformity of the renal pelvis and calyces, and the presence of a ureteropelvic stricture.

The pelvis was greatly distended by a large intrapelvic mass, which proved to be a large papilloma with malignant changes at its base, and was reported by the Massachusetts Tumor Diagnosis Service as epidermoid carcinoma. A two-stage nephroureterectomy was performed. The ureter showed no involvement.

The patient was apparently well 1½ years after the operation, but there has been no follow-up cystoscopic examination to check the possibility of bladder implants. The urine was negative except for the slightest possible trace of albumin.

The evidence in this case is, of course, somewhat presumptive, but it seems reasonable to suppose that sometime during the thirty-one-year period of recurrent left renal pain it would have been possible to remove this kidney in its precancerous state.

Sir Thomas Lewis* has said of pulsus alternans: "It is the faint and anguished cry of a fast failing muscle, which, when it comes, all should strain to hear, for it is not long repeated. A few months, a few years at most, and the end comes." This clinical metaphor may well be applied to renal pain, for though the latter requires no straining for an audition when it comes, it too is the anguished cry of an organ that is failing, or may fail. And having been heard, it should be heeded; for, unlike the helpless voice of pulsus alternans, this voice is a cue which may render possible the rescue of an organ or an individual from an insidious death.

SUMMARY

The end results of four cases in which renal pain was allowed to recur unheeded are herein illustrated. That these cases came to light on a small urological service within a short period of time suggests the number of similar cases which probably occur in the country at large.

With this in mind, a reiteration of the results of failure to investigate renal pain appears to be warranted.

32 Summer Street.

*Lewis, T.: *Clinical Disorders of the Heart Beat*. Sixth edition. 131 pp. London: Shaw & Sons Ltd., 1925. P. 121.

CLINICAL NOTE

AN INGESTED FOREIGN BODY IN THE BUTTOCK*

Report of a Case

PERCY A. BROOKE, M.D.†

WORCESTER, MASSACHUSETTS

INJURIES to the lower part of the rectum and anal canal from foreign bodies are caused either by objects' being introduced into the rectum by way of the anus or by injurious substances or articles ingested with certain foods.

A review of the literature of the last twenty years has shown a fairly large number of papers dealing with foreign bodies in the rectum. Most of these report the actual presence of foreign bodies in the rectum rather than give information as to the damage that can be inflicted by them on the rectum, anus and surrounding tissues. The majority of objects referred to in these reports had been inserted into the rectum from below and were found free in it. So far as I know, there are no cases on record in which an ingested foreign body had pierced the rectal or anal walls and lodged in the tissues external to the rectum.

Two cases are cited, however, in which foreign bodies introduced into the rectum were found in the perirectal tissues and not in the lumen. Sayers[1] removed a wooden penholder from an abscess in the tissues adjacent to the coccyx, the object having been introduced into the rectum by the patient as an erotic act. Landsman[2] cited a case of encysted foreign body in the rectum that was mistaken for a malignant tumor.

This paper reports a case of a localized abscess,

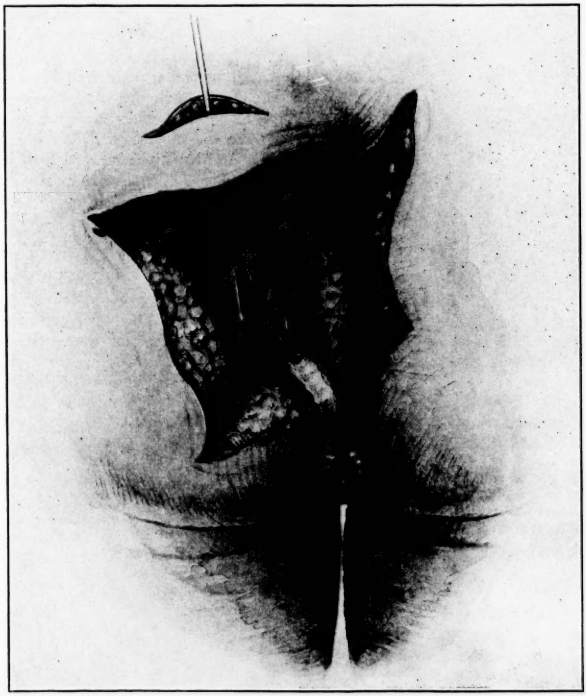


FIGURE 1.

*From the Department of Proctology, Worcester City Hospital.

†Proctologist, Worcester City Hospital and Memorial Hospital, Worcester.

an anal fistula and an encapsulated mass, somewhat superficial and posterior to the left ischiorectal space, subsequent to the ingestion of a chicken bone. The foreign body was found in the tissues of the buttock in a glistening, encapsulated cavity, which had been ruptured by a recent injury to the tissues superficial to the cavity.

Case Report

A 47-year-old woman called to see Dr. N. S. Scarcello, of Worcester, complaining of tenderness in the left buttock, which was preceded by a fall 2 days previously. The patient was advised to take hot sitz baths. About 1 week later she said that the night before she had had chills and felt feverish, and that a painful lump had developed near the point she struck when she fell. The patient was referred to me on October 31, 1939.

Examination revealed a large, brawny, indurated area in the left buttock about 4 cm. from the anal margin and posterior to the position of the left ischiorectal space. At the mucocutaneous line in the left posterior quadrant was a hypertrophied papilla and a patent crypt, into which a bent probe could be easily inserted. The temperature was 102°F. The patient was sent to the Worcester City Hospital.

Under spinal anesthesia an incision was made into the indurated area and a considerable amount of yellowish, creamy pus was evacuated. The resulting cavity did not penetrate deep into the ischiorectal space, but extended posterior to and lateral from it. A fistulous tract was discovered having its origin in the crypt mentioned above and extending laterally toward the cavity for 3 cm. There an encapsulated mass 6 cm. long and 2 cm. wide was found. Projecting from the medial end of this mass was the end of a chicken bone (Fig. 1). After the mass had been opened the bone was removed. It measured 5 cm. long, and one end was shaped like a harpoon. It was evidently the top part of the breast bone. The inside of the mass was glistening and reddish white. Originating in the cavity were several tracts. These were opened up and the overlying tissue was removed, since it appeared to be very abnormal. At the top part of the encapsulated orifice was a passage into which a probe was inserted. This probe proceeded outward for 3 cm. and then approached the surface. A stab wound was made in the skin and the probe reached the surface at this point.

The usual aftercare was carried out, and 6 weeks after the operation the cavity had closed and all the wounds had healed.

The patient denied having inserted any foreign body into the rectum, and there was no apparent reason for doubting her story. On the other hand, she did not remember having swallowed a bone.

The discovery of foreign bodies in the rectum is not unusual. It has been pointed out that mode of entrance is more frequently from below than by way of the gastrointestinal tract. There are three things about this case that make it unusual: first, that it was possible for a person to swallow a chicken bone 5 cm. long and sharp at both ends and not be aware of the fact; secondly, that this object traversed the entire gastrointestinal tract, apparently without doing harm, and pierced the lower rectal and anal walls without discomfort to the host; and thirdly, that the foreign body re sided in an encapsulated cavity which failed to cause the slightest bit of trouble to the host until she fell and ruptured the capsule.

Summary

The case is reported of an ingested chicken bone removed from the tissues of the left buttock. The bone traversed the entire gastrointestinal tract and pierced the rectum immediately above the mucocutaneous line. Six weeks after operation the wound had completely healed.

27 Elm Street.

References

1. Sayers, J. R.: Foreign body in rectum with subsequent passage through lower gluteal muscles (sacro-coccygeal region). *U. S. Nav. M. Bull.* 30:51, 1932.
2. Landsman, A. A.: Encysted foreign body of the rectum mistaken for malignant tumor. *Transactions of the American Proctologic Society, 30th Annual Session, Detroit, May 13-15, 1929.* P. 29.

REPORT ON MEDICAL PROGRESS

PHYSIOLOGY*

HEBBEL E. HOFF, M.D.†

NEW HAVEN, CONNECTICUT

THREE publications merit mention as indications of progress in physiology. The first is the twentieth volume in the series of research publications of the Association for Research in Nervous and Mental Disease,[1] devoted this year to the hypothalamus and central levels of autonomic function. A large volume of nearly a thousand pages, it is divided almost equally into sections on anatomical, physiological and clinical studies. A very complete bibliography is included, as well as a short historical account by Fulton. Fröhlich's original description of the adiposogenital syndrome is reprinted; it might have been made more accessible by translation into English. The second book is the short monograph by Barnes[2] entitled *Electrocardiographic Patterns*. Based on material presented at the meeting of the American Medical Association in 1937, it is notable for the careful correlation of electrocardiographic tracings, clinical history and pathologic findings. It exercises a valuable influence in insisting on the study and evaluation of all the various leads in the diagnosis of cardiac infarction, rather than dependence on some unusual lead of supposedly special virtue. The monograph is noteworthy for the clearness and good use of illustrations, and for the introduction in a later chapter of the subject of the electrocardiogram in pericarditis.

The *Selected Writings of Sir Charles Sherrington* issued under the editorship of Denny-Brown,[3] is a particularly well-planned tribute to Sir Charles Sherrington. It outlines the history of his researches in the words of some of his most significant accomplishments, and represents in reality the history of an era in neurophysiology. Sherrington's pupils will find the volume an old friend, and will wish only that still more of the story could have been told, and many more excerpts included. To all physiologists and neurologists it will increase the availability of the writings of Sherrington, which constitute so much of the past and so much of the foundation for the future.

THE "RESPIRATORY CENTER"

It has been generally accepted that the rhythmic movements of respiration are initiated by the automatic activity of a bilateral group of cells lying in the medulla. These cells have been considered to act as a sort of pacemaker for respiratory activity in much the same fashion as the sinoauricular node acts as the pacemaker for the heart, and they are classically — and loosely — termed the "respiratory center." The work of Bronk and Ferguson[4] indicates the general nature of this nervous discharge: Each contraction in an inspiratory or expiratory muscle is the result of a short burst of impulses in each motor unit; variations in depth of respiration are the result of variations in the frequency of discharge from the individual nerve cells, the duration of this discharge and the number of nerve cells in action. The discharge of impulses in expiratory and inspiratory neurones is under reciprocal control, so that the two alternate phasically. This discharge continues after the vagus nerves have been cut and phasic proprioceptive impulses have been interrupted by curarization. Gesell[5,6] has shown that neurones in the medullary respiratory center originate this activity. He has summarized the evidence in support of the view that these neurones are spontaneously rhythmic, and are truly the pacemaker of the respiratory rhythm. Normal rhythmic activity continues after procedures that seem completely to deafferent the respiratory center, namely section of the vagus, deafferentation of cervical and cranial nerves or complete curarization, which stops phasic activity in the muscle proprioceptors. A very strong argument in favor of spontaneous rhythmicity of the respiratory center is the observation by Adrian and Buytendijk[7] of slow rhythmic potential changes in the isolated brain stem of the goldfish, which closely parallel the respiratory rhythm in the intact fish.

There is, however, evidence that the origin of respiratory rhythm is not so simple as this, and it is furnished largely by recent review of the very interesting papers of Marckwald[8,9] in 1887 and 1890. Stella[10] and especially Pitts, Magoun and Ranson[11–13] deserve credit for calling attention to the significance of Marckwald's observations. The experimental evidence, in the essentials of which all these authors agree, may be stated briefly: There is, in the medulla, a bilateral group of cells over the inferior olive which controls inspiration.

*From the Laboratory of Physiology, Yale University School of Medicine.
†Associate professor of physiology, Yale University School of Medicine.

Stimulation of this inspiratory center produces inspiratory effort, continuing as long as the stimulation is maintained. The animal may be killed by asphyxia by thus throwing it into a prolonged inspiratory spasm. Slightly above the center for inspiration is an expiratory center, where stimulation produces a maintained expiration. The decerebrate cat breathes practically normally, even when the vagi are cut. If the section of the brain stem is made at a somewhat lower level, namely just below the upper part of the tegmentum of the pons, but still well above the medullary respiratory center, the animal breathes normally so long as the vagi are intact. When the vagi are then cut, or blocked by cold, the animal goes into a prolonged inspiratory spasm. Although this inspiratory spasm ("apneusis") may occasionally be broken by short pauses, there is no appreciable expiration, and the animal dies from asphyxia.

From these experiments Pitts, Magoun and Ranson conclude that the medullary respiratory center is not spontaneously rhythmic, but if completely isolated from outside influence gives rise to a constant discharge from the inspiratory center, the intensity of which depends on the carbon-dioxide content of the arterial blood[14]; and that this constant discharge is periodically inhibited in one or both of two ways. Afferent impulses in the vagus, arising because of the stretch of the bronchi in inspiration,[15] may serve to convert the constant into an intermittent discharge. There is also a center higher up the brain stem, presumably in the upper part of the tegmentum of the pons, which can do the same thing. Either the vagus or the pontine center may alone operate to render periodic the constant activity of the medullary respiratory center. The pontine center does not seem to be influenced reflexly, and it is still problematical how it operates to produce the periodicity it imposes on the primitive respiratory center. It may again be spontaneously rhythmic, and there is evidence from the work of Gasser that single nerve fibers may give rise to this type of periodic activity.[16] On the other hand, Pitts, Magoun and Ranson decide on anatomical grounds that there is probably a reciprocal relation between the medullary inspiratory center and the pontine center, so that activity in the one inhibits the other, and vice versa, and a type of "circus movement" is set up which keeps the two centers in a state of alternating activity. Whatever the explanation, these experiments are of the greatest importance in calling renewed attention to the existence of a brain-stem center lying above the medulla, which must now logically be considered as an integral part of the "respiratory center."

The Origin of Phasic Movements

An interesting counterpart of the work reported here on the rhythm of the respiratory center is found in recent papers by Smith, Mettler and Culler.[17, 18] These workers found that in the cat two types of response may be elicited by faradic stimulation of the cerebral cortex, a phasic and a tonic reaction. They report that the phasic type of response can be elicited only in an animal in which the dorsal roots as well as the ascending ventral spinocerebellar tracts are intact. When this afferent pathway is interrupted, stimulation of the cortex yields only a tonic or maintained contraction. They conclude that the stimulation of the cortex sets up a constant discharge from the neurones in the motor root unless it is periodically inhibited by impulses originating in the muscle proprioceptors.

This view, as the authors themselves point out, is at variance with evidence concerning other phasic movements. Sherrington[19, 20] noticed in 1906 that the scratch reflex in the decerebrate or decapitate dog and cat proceeds even more briskly than normal after the limb has been deafferented. Graham Brown[21] demonstrated that phasic running movements may be initiated in an isolated spinal segment that is completely deafferented. It is, of course, a matter of observation that phasic movements may be executed by the tabetic limb, and monkeys execute phasic movements with hind limbs that have been deprived of sensation by appropriate section of the dorsal roots.

Muscle Hemoglobin

A review by Millikan[22] on muscle hemoglobin calls attention to an important place of respiration not always sufficiently emphasized. This substance, closely related to the hemoglobin in blood, is partly responsible for the red color of muscles, and differences in its concentration are responsible for the difference between "pale" and "red" muscles. It has been known for some time that distinct differences in physiologic behavior are associated with the difference in color of the muscle. Red muscles operate more slowly, maintain contractions over longer periods with less fatigue than do pale muscles, and have a slower time of reaction. Examples of red muscles are the heart muscle of large mammals, the wing muscles of large flying birds and the leg muscles of running animals, such as the horse and the dog. Muscles which contract more frequently have less hemoglobin and are pale. An extreme example is the wing muscle in flying insects, which may contract as often as three hundred times per second. The hearts of small birds and small mammals,

such as mice, also contain smaller quantities of hemoglobin. Some muscles, such as the heart and leg muscles of the frog, contain no muscle hemoglobin. In the cat, one of the muscles of the calf (soleus) is red while the other (gastrocnemius) is pale. The twitch of the soleus muscle is more prolonged, it gives a more smoothly fused tetanus, full tetanus is maintained with fewer impulses per second, and it fatigues less readily. It is therefore fitted for economical maintenance of tension over long periods of time, as in standing. The gastrocnemius muscle, on the other hand, gives a shorter but more vigorous twitch, and is consequently adapted for short acting but strenuous activity, such as running. The same muscle may show a gain in muscle hemoglobin following increased activity.

The concentration of muscle hemoglobin is much less than that of hemoglobin in the blood. Thus the maximum concentration of muscle hemoglobin in the heart of the dog is nearly 500 mg. per 100 gm. of tissue, while the concentration in the blood may be as high as 18,200 mg. per 100 gm. The total oxygen capacity of all the muscle hemoglobin in a man has been calculated at 345 cc., while the blood could hold 1160 cc.[23] Millikan has calculated that in the normal dog's heart the amount of oxygen available in combination with muscle hemoglobin would be used up in about seven seconds of normal activity, or in less than a second of extreme activity. The substance is obviously therefore able to act only as a short-time source of oxygen.

The properties of muscle hemoglobin favor its storage function. It has a greater affinity for oxygen than has blood hemoglobin, so that, even at the venous end of the capillaries, stores of muscle hemoglobin will be full while the blood will be seriously depleted of oxygen. On the other hand, it appears that the cell oxidase systems can on their part operate at a still lower oxygen tension, and in turn deplete the oxygen stored in muscle hemoglobin.

The ability of muscle hemoglobin to store oxygen and deliver it to the cells at a later time seems now to explain the unusual ability of some animals to dive for prolonged periods. Men and other non-diving mammals can hold their breath for only a minute or so if respiration is shut off without any preparation. Here the limiting factor is probably the accumulation of carbon dioxide. When the breath is held after a period of forced breathing, respiration can be suspended for as much as five minutes or slightly longer. The limiting factor is the oxygen capacity of the body, and it can be calculated that the breath can be held only as long as it takes to use up the oxygen in the blood, tissue fluids, lungs and muscle hemoglobin. If the lungs are filled with pure oxygen after forced breathing, three or four liters more of oxygen are made available, and some experimenters have been able to hold their breaths for as long as fifteen minutes.

These are relatively short periods when compared with times for diving mammals. Some whales may remain submerged for two hours, and seals, muskrats and beavers regularly make dives of fifteen minutes. It must also be remembered that they do not remain at rest, but may show considerable activity. At least one clue to this behavior is the discovery by Robinson[24] that the muscle of the seal contains eight to ten times as much muscle hemoglobin as is found in the muscle of non-diving mammals. Irving[25] has discussed the other mechanisms that may also operate to facilitate endurance while diving.

Millikan's work makes necessary a reconsideration of the generally accepted views concerning the chemistry of muscular contraction. These hold that the energy for muscular contraction is derived principally from the anaerobic breakdown of certain substances found in muscle, and that during rest these compounds are resynthesized, with energy derived from oxidation. The process may be likened to a storage battery, which provides a readily available source of energy, but must be recharged between periods of use. Three separate anaerobic reaction systems have been postulated as the source of the energy for contraction. The first of these was the breakdown of glycogen to lactic acid. Later Lundsgaard[26] showed that contraction still occurred after the breakdown of glycogen to lactic acid was prevented by poisoning the muscle with iodoacetic acid, and proposed the hydrolysis of phosphocreatine as the source of the energy. Still later the hydrolysis of adenosine triphosphate was suggested as the primary process. In recent years Sacks and Sacks[27] have brought forward certain objections to the theory of anaerobic mechanisms, and have proposed that the fundamental reactions in contracting muscle are oxidative and not anaerobic, and that anaerobic reactions take place only when the oxygen supply is inadequate to support a fully aerobic metabolism. Their arguments are based largely on the time required to resynthesize the precursors of the anaerobic metabolites. Naturally, the rate of resynthesis of these substances must be rapid enough so that it can account for their nonappearance during light exercise with an adequate oxygen supply. Actually, the lactic acid cycle does not meet these requirements, and in fact a muscle

with an intact blood supply does not resynthesize lactic acid at all, but lets it escape into the circulation to be resynthesized in the liver or the heart. Sacks[27] has recently demonstrated that oxidative resynthesis of the other two substances does not proceed fast enough to permit the establishment of the "steady state."

Millikan has now been able to show that muscle hemoglobin begins to give up its oxygen within a fifth of a second after the onset of tetanic contraction, and fully regains it in a few seconds after cessation of the contraction in the presence of an adequate blood flow. This rapid utilization of oxygen seems to account for the greater part of the total oxygen demands of the contraction. Millikan concludes:

> The acceptance of these results does not necessarily mean the abandonment of the classical theory of anaerobic contraction and oxidation recovery. It does, however, mean something nearly as catastrophic, namely that none of the reactions of anaerobic muscle biochemistry seem to be of much importance for aerobic activity. The theory that a direct oxidative process provides the energy for contraction was proposed by Sacks in 1932. Since the ability of muscles to operate for a time anaerobically is unquestioned, this hypothesis requires a dual mechanism: one, a normal aerobic, quick, efficient mechanism; the other, an emergency, oxygen-debt mechanism, presumably of lower efficiency, called into action when there is an oxygen lack. In terms of the well-known analogy, the muscle can run off its batteries if it has to, charging them up afterwards, but it prefers to operate by direct drive if it can.

Heparin

The monograph on heparin by Jorpes[28] calls attention to renewed interest in a substance that has been known as a potent anticoagulating agent since its discovery by Howell in 1916, but which has only recently been made available for extensive study by the improved methods of recovery developed by Charles and Scott and cited by Best.[29] Named heparin because of its abundant occurrence in the liver, it is now known to be present throughout the body. It unites in vitro and in vivo with highly basic dyes, especially toluidine blue. With this dye it gives a strong purple stain in vivo, and the dye can therefore be used to stain histological preparations and detect its presence. This technic shows that heparin is present in large quantities in the mast cells of Ehrlich, and it is presumed that these cells secrete the material into the blood stream. This possibility seems strengthened by the position of the mast cells around the capillaries and small nonmuscular blood vessels.

The anticoagulating activity of the most recent crystalline compounds is about 100 units per milligram, that is, 1 mg. will protect 100 cc. of blood from coagulation for twenty-four hours. In man, 1 mg. per kilogram of body weight will prolong the coagulation time to twenty or thirty minutes. There is still some question about the harmlessness of the substance. In dogs it has been difficult to detect any harmful effects, even when administered in large quantities over several days. In man it has been used extensively, with few untoward results, but there are some reports of arterial hemorrhages following its use.

The mechanism of the action of heparin is still disputed.[30] Howell's original conclusion was that it prevented the activation of prothrombin, but there are some workers who claim that it prevents the reaction between thrombin and fibrinogen.[31] Wherever it may function, there seems to be general agreement that it acts because of its high electronegative charge. This view is supported by the discovery of anticoagulant activity in other compounds of great molecular weight possessing high ionic charges.

Heparin has not yet been assigned any definite function in the normal organism, although the situation of the mast cells suggests that it may act to prevent thrombus formation in the small vessels. It may also operate to maintain the fluidity of other body fluids. The liberation of heparin into the blood stream in peptone shock in dogs has been shown to cause the increased coagulation time in this condition.

Clinically heparin has been used in a variety of conditions; obviously its employment has been at times injudicious, especially when the not too remote possibility of arterial hemorrhage has not been kept in mind. There is, however, an obvious reason for its employment in diseases complicated by thrombosis. Here the damage caused by the lesion responsible for the thrombus formation may be relatively unimportant, while the real damage is done by growth of the thrombus or by embolism. Some of these circumstances are reviewed by Jorpes and by Best.[29] More recently Kelson and White[32] have reported successful treatment of subacute bacterial endocarditis by the combined use of heparin and sulfapyridine. The definite possibility of cerebral hemorrhage[33] cannot be considered a contraindication to this treatment in a disease that has previously been invariably fatal.

The Cardiovascular System

An excellent paper by Blumgart, Schlesinger, and Davis[34] contributes basically to the anatomy, physiology and pathology of the coronary circulation, and presents a unified concept of the clinical manifestations of inadequate cardiac circulation. Extending the earlier observations from the same laboratory, this paper arrives at the following con-

clusions: In normal hearts the coronary arteries are anatomically and physiologically end arteries. While smaller vessels have rich anastomoses with one another, as shown by the ready passage of watery injection materials from one coronary artery to another, the failure of mixing when more viscous injection masses are employed demonstrates the absence of anastomoses of a diameter of 40 microns or greater. There is no development of anastomoses with age, in the absence of disease of the coronary arteries. Obstruction to normal coronary arterial blood flow by narrowing or occlusion results regularly in the development of intercoronary anastomoses measuring 40 to 200 microns in diameter. These anastomoses may compensate so well for the deficiency in coronary supply that the circulation remains adequate for ordinary activities, and no signs of necrosis or infarction can be found. Myocardial infarction results from a disproportion between the demand for blood and its supply. It may be produced by an excessive demand for blood in the presence of a reduced supply adequate for normal demands, or may follow reduction of blood supply below even minimal demands. The absolute necessity for immediate and complete bed rest, sedation, reduction of excessively high heart rate and other measures designed to reduce the work of the heart in coronary occlusion is emphasized as a measure that may very possibly limit greatly the extent of myocardial necrosis, or even prevent its development. Lack of oxygen supply to the myocardium may develop following causes other than narrowing or occlusion of the coronary vessels, for example fall in blood pressure, as in shock, and lack of oxygen-carrying capacity of the blood, as in anemia. These factors must be closely watched in patients whose coronary insufficiency renders them more than usually vulnerable to oxygen lack. In addition to these and other very important considerations, the paper raises a great many questions to be answered only by future work. The mechanism of development of the arterial anastomoses and the rate at which they become established are important points about which the authors will no doubt have more to say in later communications.

The fertile suggestions of Goldblatt continue to dominate the study of renal hypertension, and much new work has been reported. Katz and Steinitz[35] have shown, by the elegant technic perfected by Hamilton, Woodbury and Vogt,[36] that renal hypertension in dogs is not accompanied by changes of the pressure in the pulmonary circulation. Rodbard,[37] working in Katz's laboratory, has shown by the ingenious procedure of anastomosis of the ureter to the lumbar vein that the normal kidney does not prevent hypertension by excreting the hypertensive substance liberated by an ischemic kidney, but antagonizes its action by virtue of its own metabolic activity. He suggests that the kidney destroys the pressor substance, but another equally possible hypothesis seems supported by two other reports. Harrison, Grollman, and Williams[38] and Page and Helmer[39] present evidence that the normal kidney secretes a substance which does not by itself alter the normal blood pressure, but will lower the pressure in renal hypertension and antagonize the action of pressor substances obtained from the kidney. Maclachlan and Taylor[40] have studied the suggestion that the hypertension which follows renal ischemia is an adaptive mechanism in which the kidney controls its blood flow in accordance with functional demands. They have been able to show that an animal with mild hypertension produced by placing one kidney in a cast and removing the other responds to an increased protein intake in the diet by an increase in its blood pressure and by an exacerbation of hypertensive symptoms.

333 Cedar Street.

REFERENCES

1. *The Hypothalamus and Central Levels of Autonomic Function.* Proceedings of the Association for Research in Nervous and Mental Disease, December 20 and 21, 1939, New York. Vol. XX. 980 pp. Baltimore: Williams & Wilkins Co., 1940.
2. Barnes, A. R.: *Electrocardiographic Patterns: Their diagnostic and clinical significance.* 197 pp. Springfield, Illinois, and Baltimore: Charles C Thomas, 1939.
3. *Selected Writings of Sir Charles Sherrington: A testimonial presented by the neurologists forming the guarantors of the journal* Brain. Edited by D. Denny-Brown. 532 pp. New York: Paul B. Hoeber, Inc., 1939.
4. Bronk, D. W., and Ferguson, L. K.: The nervous control of intercostal respiration. *Am. J. Physiol.* 110:700-707, 1935.
5. Gesell, R.; Bricker, J., and Magee, C.: Structural and functional organization of the central mechanism controlling breathing. *Am. J Physiol.* 117:423-452, 1936.
6. Gesell, R.; Atkinson, A. K., and Brown, R. C.: The origin of respiratory activity patterns. *Am. J. Physiol.* 128:629-634, 1940.
7. Adrian, E. D., and Buytendijk, F. J. J.: Potential changes in the isolated brain of the goldfish. *J. Physiol.* 71:121-135, 1931.
8. Marckwald, M.: Die Athembewegungen und deren Innervation beim Kaninchen. *Ztschr. Biol.* 23:149-283, 1887.
9. *Idem:* Die Bedeutung des Mittelhirns für die Athmung. *Ztschr. Biol.* 26:259-289, 1890.
10. Stella, G.: On the mechanism of production, and the physiological significance of "apneusis." *J. Physiol.* 93:10-23, 1938.
11. Pitts, R. F.; Magoun, H. W., and Ranson, S. W.: Localization of the medullary respiratory centers in the cat. *Am. J. Physiol.* 126:673-688, 1939.
12. *Idem:* Interrelations of the respiratory centers in the cat. *Am. J. Physiol.* 126:689-707, 1939.
13. *Idem:* The origin of respiratory rhythmicity. *Am. J. Physiol.* 127:654-670, 1939.
14. Stella, G.: The dependence of the activity of the "apneustic centre" on the carbon dioxide of the arterial blood. *J. Physiol.* 93:263-275, 1938.
15. Adrian, E. D.: Afferent impulses in vagus and their effect on respiration. *J. Physiol.* 79:332-358, 1933.
16. Gasser, H. S.: The control of excitation in the nervous system. *The Harvey Lectures: Delivered under the auspices of the Harvey Society of New York, 1936-37.* Series 32. 245 pp. Baltimore: Williams & Wilkins Co., 1937. Pp. 169-193.
17. Smith, C. G.; Mettler, F. A., and Culler, E. A.: The phasic response to cortical stimulation. *J. Neurophysiol.* 3:182-187, 1940.
18. Mettler, F. A.; Smith, C. G., and Culler, E. A.: The role of afferent impulses in the response to cortical stimulation. *Am. J. Physiol.* 129:423P, 1940.
19. Sherrington, C. S.: Observations on the scratch-reflex in the spinal dog. *J. Physiol.* 34:1-50, 1906.
20. *Idem:* Notes on the scratch-reflex of the cat. *Quart. J. Exper. Physiol.* 3:213-220, 1910.
21. Brown, T. G.: Studies in the physiology of the nervous system. XII. Rhythmic responses in the simple reflex-progression-scratch. *Quart. J. Exper. Physiol.* 6:25-56, 1913.
22. Millikan, G. A.: Muscle hemoglobin. *Physiol. Rev.* 19:503-523, 1939.

23. Johnson, R. E.; Forbes, W. H.; Dill, D. B., and Henderson, L. J.: Respiration. *Ann. Rev. Physiol.* **2**:21-44, 1940.
24. Robinson, D.: The muscle hemoglobin of seals as an oxygen store in diving. *Science* **90**:276, 1939.
25. Irving, L.: Respiration in diving mammals. *Physiol. Rev.* **19**:112-134, 1939.
26. Lundsgaard, E.: Untersuchungen über Muskelkontraktionen ohne Milchsäurebildung. *Biochem. Ztschr.* **217**:162-177, 1930.
27. Sacks, J.: Recovery from muscular activity and its bearing on the chemistry of contraction. *Am. J. Physiol.* **122**:215-223, 1938.
28. Jorpes, J. E.: *Heparin: Its chemistry, physiology, and application in medicine.* 87 pp. New York and London: Oxford University Press, 1939.
29. Best, C. H.: Heparin and thrombosis. *Brit. M. J.* **2**:977-981, 1938.
30. Ferguson, G. H.: Blood: coagulation, biophysical characters, and formed elements. *Ann. Rev. Physiol.* **2**:71-108, 1940.
31. Glazko, A. J., and Greenberg, D. M.: The mechanism of the inhibiting effect of electrolytes and heparin on blood coagulation. *Am. J. Physiol.* **128**:399-407, 1940.
32. Kelson, S. R., and White, P. D.: A new method of treatment of subacute bacterial endocarditis. *J. A. M. A.* **113**:1700-1702, 1939.
33. Friedman, M.; Hamburger, W. W., and Katz, L. N.: Use of heparin in subacute bacterial endocarditis. Preliminary report. *J. A. M. A.* **113**:1702, 1939.
34. Blumgart, H. L.; Schlesinger, M. J., and Davis, D.: Studies on the relation of the clinical manifestations of angina pectoris, coronary thrombosis, and myocardial infarction to the pathologic findings. *Am. Heart J.* **19**:1-91, 1940.
35. Katz, L. N., and Steinitz, F. S.: Pulmonary arterial pressure in experimental renal hypertension. *Am. J. Physiol.* **128**:433-439, 1940.
36. Hamilton, W. F.; Woodbury, R. A., and Vogt, E.: Differential pressures in the lesser circulation of the unanaesthetized dog. *Am. J. Physiol.* **125**:130-141, 1939.
37. Rodbard, S.: Elimination of the chemical mediator of renal hypertension by renal metabolism. *Am. J. Physiol.* **129**:448P, 1940.
38. Harrison, T. R.; Grollman, A., and Williams, G. R., Jr.: The antipressor action of renal extracts and their capacity to reduce the blood pressure of hypertensive rats. *Am. J. Physiol.* **128**:716-724, 1940.
39. Page, I. H., and Helmer, O. M.: Angiotonin-activator and renin and angiotonin inhibitor. *Am. J. Physiol.* **129**:435P, 1940.
40. Machlachlan, I., and Taylor, N. B.: The effect of diet upon renal hypertension. *Am. J. Physiol.* **129**:413P, 1940.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26231

PRESENTATION OF CASE

First Admission. A thirty-eight-year-old building inspector was admitted to the hospital complaining of dyspnea on exertion of nine weeks' duration.

Three years before this first admission (twelve years before his death) two teeth became "infected" and the joints of both ankles and knees became exquisitely tender to pressure and motion. All his teeth were removed and a few weeks later his illness cleared, but complete recovery required six months. He was well until about nine weeks before his first admission, when he suddenly became dyspneic and felt exhausted while climbing three flights of stairs to his home. He ate supper and immediately noted a feeling of great epigastric distention. He went to bed and fell asleep. Three hours later he awoke with a knifelike pain in the epigastrium over an area measuring 8 to 10 cm. After about two hours the pain shifted to the lower abdomen and radiated to the right groin and right testicle but disappeared in about six hours. A physician gave him digitalis. A second identical attack occurred three weeks later. A third attack occurred two days before admission, and he vomited every two hours for about twenty-four hours. The vomitus was clear and had no taste. There were no other symptoms. A tonsillectomy and adenoidectomy were performed three weeks before admission.

The family, marital and past histories were non-contributory.

The physical examination revealed a well-developed and slightly obese man propped up in bed in moderate respiratory distress. The skin was warm and dry and showed numerous telangiectatic spots scattered over the abdomen and trunk. No definite petechiae were seen. The scleras were clear. He was pale with slight cyanosis and a cyanotic flush over the cheeks. The throat was injected, and the tonsils were absent. The chest showed a prominence of the left side, and a precordial impulse was definitely visible in the axilla. The apex of the heart was definitely enlarged toward the left in the anterior axillary line, and there was slight enlargement toward the right with some widening of the supracardiac dullness. The rate was rapid, absolutely irregular, with a pulse deficit which prevented accurate timing of murmurs. The force of the beat varied in intensity. The first heart sound was partially obliterated by a rough, short presystolic and a systolic apical murmur. The second sound was reduplicated and clicking, but there were no murmurs at the pulmonic or aortic areas. The peripheral vessels were negative to palpation. The blood pressure was 160 to 120 systolic, 105 to 70 diastolic. The lungs showed many moist rales at both bases, especially the left; but the breath sounds were otherwise normal. The remainder of the examination was negative.

The temperature was 100.2°F., the pulse at the apex 140 and at the wrist 86. The respirations were 25.

Examination of the blood showed a red-cell count of 4,600,000 with a hemoglobin of 70 per cent (Sahli), and a white-cell count of 20,800 with 85 per cent polymorphonuclears; the smear was normal. Urine examinations showed + albumin, 35 to "rare" red blood cells and 10 to 5 white blood cells per high power field in the sediment, with occasional granular and hyaline casts. The stools were negative. The blood Hinton and Wassermann tests were negative. The serum nonprotein nitrogen was 33 mg. per 100 cc.

The patient was digitalized, though it was stated that he did not respond in the "usual way" in that the ventricular rate was difficult to control. With bed rest and supportive care, the temperature fell to normal on the fifth day. There was a slight pulse deficit, but otherwise he seemed improved and was discharged on the fifteenth hospital day.

Second Admission (five years later). Following discharge the patient was well and active until six months before his second hospital admission when he developed recurrent furuncles and abscesses involving the neck and buttocks.

Physical examination now showed a soft blowing diastolic murmur along the left sternal border in addition to the other findings noted above. Except for a white-cell count of 14,000, the laboratory findings were normal. A sugar-tolerance test was normal. He was discharged on the seventh day after dermatological therapy.

Third Admission (six weeks later). He was admitted for treatment of a rectal fissure which was successfully excised without complications.

Fourth Admission (fifteen months later). The patient entered with a "respiratory infection." Sticky rales were heard over the left lower chest, but no heart failure signs were elicited. With bed rest, a slightly elevated temperature fell to normal, and he was discharged after one week's stay in the hospital.

Final Admission (three years later, twelve years after the onset of his first symptom). Seven months before this admission, the patient noted the sudden onset of severe right costovertebral pain, which radiated to the right groin and to the right testicle. The pain was severe and associated with nausea and vomiting; it was of a cramplike or stabbing nature and remained almost constant for two days and then gradually disappeared, with some residual soreness. There was no dysuria or hematuria. Following this episode the patient was well until the day before admission, when he again had the onset of severe right flank pain. At this time it remained high and did not radiate to the testicle. The pain was again stabbing, severe, and associated with nausea and vomiting. It was almost constant until he was given a hypodermic injection for relief. He was then admitted to the hospital for study.

Physical examination revealed a well-developed and well-nourished plethoric man complaining of spasms of right flank pain referred to the suprapubic regions. The heart apex was seen and percussed at a level 4 cm. beyond the midclavicular line in the fifth interspace. The rhythm was totally irregular, but there was no pulse deficit. There was a rough systolic murmur at the apex with a loud, late, long, presystolic murmur also at the apex. A rough low-pitched systolic murmur was heard at the aortic area, and a moderately loud blowing diastolic murmur was present along the left sternal border. The pulmonic second sound was much louder than the aortic second sound. No thrills were felt. The blood pressure was 166 to 120 systolic, 80 diastolic. There was no evidence of congestive failure. Tenderness was elicited in the right costovertebral angle with protective muscular spasm. There appeared to be slight tenderness over the course of the ureter to a point just above the pelvic brim. The spleen and liver were not palpable.

Examination of the blood showed a red-cell count of 5,400,000 with a hemoglobin of 15 gm. (photoelectric-cell technic) and a white-cell count of 9800 with 77 per cent polymorphonuclears. Examination of the urine showed albumin which varied from ++ to +++. The urine concentrated normally up to 1.022. The sediment of all the specimens contained a few red blood cells. The nonprotein nitrogen was 65 mg. per 100 cc. Intravenous pyelograms on the sixth hospital day showed no evidence of excretion of the dye on either side. A barium enema was negative.

On the eighth hospital day he was awakened by pain poorly localized under the left ribs and in the left upper quadrant. It was cramplike in character and seemed to be related to gas. Palpation revealed no unusual masses or tenderness. No friction rubs were heard. Two hours later his condition became rapidly worse; the outstanding signs were those of peripheral shock. He was cold and sweaty. The blood pressure rose temporarily to 220 systolic, 80 diastolic and later subsided to its previous level. Numerous medium rales appeared over the upper chest on both sides, most prominent below the clavicles. There were slight impairment of resonance, and increased tactile fremitus and whispered voice. The lung bases remained relatively clear. In spite of the abrupt appearance of these signs in the lungs, there was no wheezing, cough or hemoptysis, no pain, and no obvious air hunger or cervical vein engorgement. The pulmonary second sound remained unchanged (moderately accentuated). A portable film of the chest showed that both upper lobes of the lungs contained a diffuse, symmetrical, mottled density extending to the apex and ending rather abruptly in the midlung field. The lower lobes were clear. The right lower lobes seemed more radiant than usual. The heart was prominent in the region of the left ventricle. There was no fluid in the pleural cavity. The white-cell count rose to 26,000. No acid-fast bacilli were found in the sputum. No new abdominal symptoms or signs appeared, but he continued to complain of rather diffuse abdominal discomfort and distention. There was no peripheral edema. The temperature rose to 101 and later to 102.8°F. on the succeeding two days. The heart action increased to 120, and increasing amounts of digitalis failed to control it. Mercupurin resulted in an output of 600 cc. in twenty-four hours. A second x-ray film showed some clearing in the left upper lobe, but there was no definite increase in the right mid-lung field and right lower lobe. A shadow in the right mid-lung field had the appearance of consolidation, whereas all the remaining shadows were consistent with edema.

He failed to respond, continued in peripheral shock, a gallop rhythm appeared, the respirations became shallow, the blood pressure dropped to 100 systolic, 80 diastolic, and the breath seemed slightly uriniferous. He quickly failed and died on the eleventh hospital day, three days after the onset of the terminal acute illness.

Differential Diagnosis

Dr. Paul D. White: "Three years before this first admission . . . two teeth became 'infected' and the joints of both ankles and knees became exquisitely tender to pressure and motion. All his

teeth were removed and a few weeks later his illness cleared, but complete recovery required six months." That sounds like past history, unless we assume that he was not well during that period; he may of course have had active rheumatism all through these three years. Thus it is a question whether this is the beginning of the present illness or whether it is past history. This sickness appears to have been rheumatic fever, probably his first rheumatic infection coming on at the age of thirty-five. Possibly it was rheumatoid arthritis, but in view of what is found later the more plausible interpretation is rheumatic fever.

There is no statement as to why his tonsils and adenoids were taken out. Evidently the tonsils were large and infected and were removed largely because of the presence of rheumatic heart disease.

Then we come to the first acute episode. He suddenly became dyspneic and exhausted. The physician who gave digitalis must have found something wrong with his heart. Dyspnea alone does not demand digitalis right away. It is likely that he developed tachycardia at the time he climbed three flights of stairs and that may have produced the dyspnea; tachycardia is produced in that way very frequently in a person with rheumatic heart disease. It was probably the onset of auricular fibrillation with rapid rate induced by effort. However, that is simply speculation at the moment. The dyspnea apparently subsided and he went to bed and fell asleep. Then came the severe, knifelike pain in the epigastrium which at first remained in that position and then shifted in a way absolutely characteristic of renal and ureteral colic because of the distribution of the pain to the right groin and testicle. Subsequent attacks occurred and each subsided quite quickly. The history does not reveal his state of health between the attacks. We may assume it was quite good and that these were isolated attacks — at intervals of three weeks first, and then of six weeks. The attacks were like renal colic, which is usually due to stones or gravel, but may possibly be ascribed to infarction from embolism.

The question that intrigues me most is the possibility of embolism producing such characteristic renal colic. I have not heard of its doing so, that is embolism to the kidney secondary to the occurrence of auricular fibrillation in the presence of heart disease and intracardiac thrombosis. It is very uncommon for the discomfort in such cases to radiate as far as the right testicle. However, we must entertain the possibility.

He was dyspneic at the time of the third attack, as he was just prior to the first attack of pain. Dyspnea may have accompanied each attack and may even have been present between attacks.

There was no statement of clubbing of the fingers.

The findings on physical examination suggest that the heart disease was of long standing. The left side of the thorax was prominent and probably had been since childhood, though there is no proof of it. We frequently see precordial thoracic bulging in the children's clinic in youngsters with big hearts due to congenital defects or to rheumatism developing in early life. There was definite cardiac enlargement. The heart may be pushed over, but if it were simply displaced the apex would be high in position and not so low as here.

We wonder whether the heart rate had been rapid right along or whether the tachycardia came only with these attacks. It is unusual to have presystolic murmurs in the presence of auricular fibrillation. The murmur may have been only mid-diastolic, or we might question its presence altogether. On the basis of these findings we have probable confirmation of the diagnosis of rheumatic heart disease with mitral stenosis, auricular fibrillation and pulmonary congestion, not necessarily due to failure but rather to the tachycardia. The heart rate was so rapid that adequate auscultation could not be carried out at that time.

Apparently there was no abdominal (or flank) tenderness, which would help to rule out a surgical abdominal emergency in this case, since he was quite alert at the time of the examination.

This man had moderate fever. It is not our experience that fever, even as little as this, is produced by congestive failure alone. There is almost always some other factor, an active infection somewhere, or infarction. There might conceivably be renal or ureteral infection due to stone, or renal infarction, or recurrent active rheumatism in a man who has had previous attacks; any of these conditions, especially active rheumatism, may precipitate auricular fibrillation, as well as cause fever.

The white-cell count was higher than we would expect from anything but moderately severe infection, or marked infarction; it was distinctly higher than we usually find with myocardial infarction or with small pulmonary infarcts.

The red and white blood cells in the urine are probably not to be explained by congestion alone. They are in keeping with renal stone or other renal disease, including infarction.

The patient was digitalized, though it was stated that he did not respond in the usual way to digitalis doses in that the ventricular rate was difficult to control. It is common to have difficulty in

controlling the ventricular rate in congestive failure in the presence of infection or infarction. A third cause for such difficulty is thyrotoxicosis of which there is no evidence here. He probably had spontaneous recovery from this acute episode. Then, I judge, the heart rate came down, because there is only a slight pulse deficit recorded thereafter. The symptoms cleared, but doubtless he still had the auricular fibrillation.

Were any x-rays of the chest, kidneys, or ureters taken at the time? Is that a permissible question for me to ask?

DR. HOWARD B. SPRAGUE: There were no x-rays taken at that time.

DR. WHITE: Any blood cultures?

DR. SPRAGUE: No. His apex rate was 75 at discharge, and the temperature was normal.

DR. WHITE: Was the pulse still irregular at discharge?

DR. SPRAGUE: Yes.

DR. WHITE: He did well apparently after this illness. There is no note of anything more until six months before his re-entry to the hospital which in a chronic rheumatic-heart patient might mean that the chronic auricular fibrillation was well controlled.

Was he continued on digitalis over that period of time?

DR. SPRAGUE: Yes.

DR. WHITE: Had the presystolic murmur become mid-diastolic at this time?

DR. SPRAGUE: It was a definite diastolic murmur at the apex.

DR. WHITE: The soft blowing diastolic murmur at the left sternal border would make one think of the probability of aortic regurgitation as an additional valve lesion.

DR. SPRAGUE: That murmur was first noted in December, 1935.

DR. WHITE: What is the time relation of that to this report?

DR. SPRAGUE: The second admission was in April, 1936. Apparently it appeared between June, 1935, and December, 1935, during which time he had gone through a period of severe carbuncles in his neck, and I noted the murmur at that time.

DR. WHITE: The heart examination would indicate the presence of mitral and aortic regurgitation, probably stenosis of both valves, though more of the mitral valve. There is one other possibility than that this aortic regurgitation had developed as a sequence to recurrent rheumatism, and that is, that syphilis may have come in, despite the earlier negative Hinton reaction, resulting in both rheumatic and syphilitic valvular disease, although we do not often see that combination. Were there new serological tests at the time, Hinton or Wassermann reactions?

DR. SPRAGUE: I think not. I do not think syphilis was a possibility.

DR. WHITE: I suspect it is not probable, but it has to be thought of.

Assuming that the technic was correct, the intravenous pyelogram showing no evidence of excretion of dye on either side, would mean that there was a good deal of kidney damage with inability to concentrate, a bad renal state, probably from many years of renal involvement.

"No friction rubs were heard." They were thinking of pleurisy due to pulmonary embolism and infarction.

"The blood pressure rose temporarily to 220 systolic, 80 diastolic. . . ." Very frequently the blood pressure in an acute episode goes up under the influence of pain or other exciting factor, even including coronary thrombosis. I have seen it higher than normal in such cases before it settles back or finally becomes quite low; a low pressure is sometimes due to rest in bed for a long period of time, rather than necessarily to a state of shock or heart failure.

"In spite of the abrupt appearance of these signs in the lungs, there was no wheezing, cough or hemoptysis, no pain, and no obvious air hunger or cervical vein engorgement." That statement does not rule out multiple pulmonary emboli. One can have embolism in the lung without any symptoms. One can have any kind of symptoms and very little in the way of signs.

Our patient had a barium enema, two chest x-ray examinations and an intravenous pyelogram. The barium enema showed nothing abnormal. A considerable portion of the terminal ileum was normal. Why was the barium enema done?

DR. SPRAGUE: The barium enema was done because the abdominal pain did not localize on one side, went from right to left, and in the past he had attacks of abdominal pain of a vague nature with some diarrhea, relieved by belladonna, and the question arose as to whether he had a lesion of the large bowel.

DR. AUBREY O. HAMPTON: The first of these chest plates that we have is the best one and shows a grossly enlarged heart. Even though this is a portable film, there is as much enlargement downward as to the left. This density in the lungs is almost exactly symmetrical, and it does end rather abruptly at the middle of the lung field. The right lower lobe is more radiant than the left, chiefly because the heart shadow is large on that side. He has one line at the dome of the diaphragm that was not described. It could be an

old scar from infarction or infection. In the films taken the following day I think you can see a fairly definite change in the chest. The left upper lobe and even perhaps the right upper lobe look clearer than before. The right lower lobe now presents the same density as the remainder of the abnormal portion of the lung. This shadow of the right border of the heart was the one assumed to be something different from the remaining shadows, but it could be dilated blood vessels superimposed upon the same general condition. It is not sharp in outline and has no really characteristic shape.

DR. WHITE: May I ask if in cases of large heart it is conceivable that there may be some unusual pressure in the lower pulmonary vessels to limit the entrance of emboli? Has it been the finding that in rare cases emboli may go only to the apices?

DR. HAMPTON: I do not think we have seen pulmonary infarction produce this picture. We have seen this picture associated with small infarcts, but this lesion is almost wholly confined to the upper lobe and it certainly would be unusual for infarction.

The intravenous pyelogram is not satisfactory from the standpoint of viewing the kidney outlines, but I think that if dye had been excreted you would have been able to see it, particularly in the bladder. The bladder contains no dye after forty minutes. It contains urine. We can say that it is normal in size.

DR. WHITE: He evidently died in shock with failure of the kidneys, heart, and lungs, but not really a great deal of heart failure. I am very much intrigued, though I probably am wrong, by the appearance of the lungs in the x-ray picture and the prominent involvement of the upper lobes; infarction can happen but is less common certainly, according to the paper by Hampton and Castleman,[1] in the upper lobes and right middle lobe. Seventy-four per cent was their figure for the location of pulmonary infarcts in the lower lobes.

DR. HAMPTON: When we found infarcts in the upper lobes we almost invariably found them in the lower lobes also.

DR. WHITE: That is the most interesting and puzzling part of the whole case, the findings in the upper lobes; infarction alone would hardly seem likely. There has also been a change in the pictures, and one would think therefore that it has not been wholly a chronic state. Bronchopneumonia would hardly seem likely to involve both upper lobes in this way, nor would tumor. Tuberculosis might, but this is not the picture of tuberculosis.

Was there any electrocardiogram?

DR. SPRAGUE: Not in the hospital records. The others were not helpful.

DR. WHITE: The best I can do is to diagnose rheumatic heart disease, probably acute as well as chronic, probably recurrent, perhaps existing all this time in a mild degree. There are some cases of long-standing rheumatic involvement — ten years or more in adults. There was in this case rheumatic involvement of both aortic and mitral valves in all probability, with less likely syphilitic aortic involvement. The heart was undoubtedly big with auricular fibrillation, on the edge of failure, and yet with very little actual congestive failure that I can find. The involvement of the lungs I first labeled pulmonary infarction with edema and terminal infection; I am now wondering if a rheumatic involvement of the lungs could account for it, a rheumatic pneumonitis, but I am not familiar with its limitation to the upper lobes. Renal calculi should be found, or extensive renal infarction, but more probably calculi, with extensive damage to the kidneys. There may have been coronary thrombosis, subacute bacterial endocarditis, pericarditis, or disease of the aorta such as dissecting aneurysm, but the evidence does not support these diagnoses.

DR. J. H. MEANS: I should like to ask Dr. Sullivan if he recalls Dr. A. Thornton Scott's findings on the distribution of edema in the lungs in cases of Bright's disease.

I recall being very much surprised, a few days ago at our Medical Grand Rounds, when Dr. Schatzki showed a film with haziness in the middle portions and apices of both lung fields, but with perfectly clear bases, and said that it looked like edema. I had supposed that edema would be most marked at the bases and least marked at the apices.

DR. EUGENE SULLIVAN: I do not recall the exact figures, but there were some cases where the pulmonary edema was not at the base, but higher up.

DR. EDWARD F. BLAND: I went over the cases with Dr. Scott, and one or two showed predominant involvement in the upper lobes. The pictures were striking and cleared rather rapidly in some cases.

DR. MEANS: Something rather like this?

DR. BLAND: Surprisingly like this.

DR. HAMPTON: A similar picture occurs in heart disease alone. I remember one case we had here some time ago with a picture quite similar to this, and it proved to be rheumatic heart disease and nothing else.

DR. SULLIVAN: One case was verified at autopsy with edema in the upper lung fields.

DR. T. DUCKETT JONES: I think what Dr. White

said about long-standing rheumatic fever and increasing heart failure for years is obvious, but how this terminal feature could be associated is difficult for me to understand. The picture and clinical story are not that of rheumatic pneumonitis. Even as vague as the syndrome is, the patient with rheumatic pneumonitis is seriously ill before symptoms appear. The majority of them would have changes detectable by x-ray study, and would have changes in the lower lobes. I should say it seems unlikely that it is a straight pneumonitis.

Dr. White: The renal condition could be the last straw.

Dr. Jones: It would have to tie up with this. You have to have something comparable to blocking off of the renal artery to explain the picture. I wonder if we could not mention a second diagnosis of rheumatic heart disease and hypernephroma which would produce pulmonary metastases.

Clinical Diagnoses

Chronic rheumatic heart disease.
Mitral stenosis and regurgitation.
Aortic regurgitation.
Congestive failure.
Auricular fibrillation.
Pulmonary edema.
Acute rheumatic fever and pneumonitis ?
Nephritis (? cause).
Uremia.

Dr. White's Diagnoses

Rheumatic heart disease, acute and chronic.
Mitral and aortic stenosis and regurgitation.
Marked cardiac enlargement.
Auricular fibrillation.
Congestive failure.
Pulmonary infarction, infection or edema (or combination thereof).
Renal and ureteral calculi or renal infarction.

Anatomical Diagnoses

Rheumatic heart disease, acute and chronic, with mitral and aortic stenosis.
Endocarditis, acute rheumatic, mitral and aortic valves.
Pericarditis, acute.
Mural thrombus, left auricular appendage.
Thrombosis of lower abdominal aorta with occlusion of common iliac vessels, lower aorta, left renal artery and superior mesenteric artery, acute.
Infarction of left kidney, acute.
Infarction of small bowel, early.
Pulmonary congestion and edema, both upper lobes.
Rheumatic pneumonitis?
Cardiac hypertrophy, involving the right ventricle and left auricle.
Hydrothorax, bilateral, slight.
Chronic passive congestion of liver and spleen.
Renal infarcts, healed, bilateral.
Cholelithiasis.

Pathological Discussion

Dr. Tracy B. Mallory: The underlying process, of course, was rheumatic heart disease. There was a greatly enlarged heart, 650 gm., and there was involvement of both mitral and aortic valves. There was a marked degree of stenosis in the mitral valve, a significant degree of stenosis and also regurgitation in the aortic. A few small fresh rheumatic vegetations were present and there was also an acute pericarditis. The coronary arteries were negative. The hypertrophy was present on both sides of the heart but more marked on the left. The lungs were rather large, very heavy, obviously edematous. On gross examination slight but poorly outlined areas of consolidation seemed palpable in the upper lobes. On microscopic examination there was no very convincing pneumonia. There was a somewhat patchy edema, quite a little atelectasis, occasional alveoli containing some fibrin and a few fibroblasts attempting to organize it, but no leukocytic infiltration. There were no fibrous plugs in the bronchi or the respiratory bronchioles such as Masson, Riopelle and Martin[2] have described in rheumatic cases, and no very extensive lobular alveolar hemorrhage such as we have seen in acute rheumatic cases. I certainly could not recognize it as rheumatic pneumonia and I doubt if it is; but I am too vague as to what the lesion is in that condition to be dogmatic. The terminal event unquestionably was a series of emboli. The main branch of the left renal artery was plugged by a fresh embolus, and small fresh emboli were found in the small branches of the right kidney. There also were scars of old infarction in both kidneys. The renal embolism must have gone back many years, and I think in retrospect, accounts for the early attacks of pain with radiation to the testicle.

Dr. White: Were there any stones?

Dr. Mallory: No. There were two more important emboli which probably precipitated death. One was to the superior mesenteric artery which was completely plugged, although the bowel had not become gangrenous. The other was a rider embolus of the aorta blocking both iliac arteries.

Dr. White: I called up a urologist to inquire whether typical renal colic *with radiation to the testicle* could be caused by renal infarction and he said he did not think so.

DR. MALLORY: Either you did not call the right urologist or his memory is short, because in this hospital they have explored patients for renal calculi and found infarction.

A PHYSICIAN: Were there any renal emboli and infarcts?

DR. MALLORY: There were a few.

REFERENCES

1. Hampton, A. O., and Castleman, B.: Correlation of postmortem chest teleroentgenograms with autopsy findings. *Am. J. Roentgenol.* 43:305-326, 1940.
2. Masson, P.; Riopelle, J. L., and Martin, P.: Poumon rhumatismal. *Ann. d'anat. path.* 14:359-382, 1937.

CASE 26232

PRESENTATION OF CASE

A fifty-six-year-old Japanese cook was admitted to the hospital complaining of dyspnea on exertion.

The patient had always been in robust health and had taken pride in his physical prowess as a wrestler and swimmer. He was thus active athletically until approximately two years before admission, when he began to tire easily. For several months before entry he noticed gradually progressing dyspnea on exertion. One month before admission he had had a bad cold, and an examination at that time by his physician revealed that his blood pressure was 130 systolic. The cold improved slowly and he seemed fairly well until the evening before entry when, immediately after supper, he experienced the sudden onset of dyspnea (without exertion), substernal oppression, but no pain or other discomfort anywhere. He opened a nearby door in an attempt to obtain more air, took soda and salt water without relief, coughed slightly, and raised moderate amounts of white frothy sputum. A physician who was called found the patient coughing and wheezing. He appeared ill and had a blood pressure of 156 systolic, 70 diastolic. He denied ever having had asthma or a similar attack before. A quarter grain of morphine sulfate was administered hypodermically, and the patient slept the night through, sitting erect. At 6 a. m. on the morning of admission he was again seen by his doctor and was found to be wheezing, with a blood pressure of 106 systolic, 60 diastolic. Examination of the heart at that time was not remarkable. Because of his symptoms he was referred to the hospital for treatment.

The family and past histories were, so far as was known, negative.

Physical examination showed a remarkably well-developed, well-nourished, muscular man who was orthopneic, dyspneic and cyanotic, with "asthmatic" wheezing respirations. He could lie flat but was uncomfortable in so doing. There were rhonchi and wheezing throughout the chest, with rales at the bases posteriorly. The vital capacity was definitely limited. The heart was slightly enlarged to percussion. The heart sounds were not well heard because of the other sounds, although they seemed to be of poor quality. A split second sound, but no murmurs, was heard over the precordium; there were no murmurs. There was no edema or ascites. The liver and spleen were not palpable. The blood pressure, which was 128 systolic, 65 diastolic, in the sitting posture, was 160 systolic, 80 diastolic in the supine position.

The temperature was 101°F., the pulse 130, and the respirations 44.

Examination of the blood showed a red-cell count of 7,500,000 with 95 per cent hemoglobin, and a white-cell count of 13,000 with 92 per cent polymorphonuclears; the smear was normal. No urine was obtained for examination. The blood Hinton test was positive, the Wassermann weakly positive. An electrocardiogram showed a normal rhythm at 105, with a PR interval of 0.18 sec., and left bundle branch block. The corrected sedimentation rate was 0.4 mm. per min., and the hematocrit reading 48 per cent.

The patient was given 10 cc. of aminophyllin intravenously, and seemed quite well and comfortable during the day of admission, with but few wheezes at both lung bases. At 1:00 a. m. the night after admission, he became mildly dyspneic. Oxygen was administered by the nurse, and the dyspnea soon cleared. At about 2:30 a. m., however, he suddenly became rapidly dyspneic and cyanotic, did not complain of pain, but attempted to remove the oxygen mask. In so doing he fell back dead.

DIFFERENTIAL DIAGNOSIS

DR. MYLES P. BAKER: It would seem to me that the burden of proof in this case lies with the man who declares this is not a case of acute coronary occlusion on the basis of sclerosis of the coronary arteries. The man's age, fifty-six, is in the decade in which clinical coronary thrombosis is most frequently observed. There have been several months of progressive exertional dyspnea without anemia, increased metabolic rate or respiratory-tract obstruction to account for the dyspnea. This is presumably cardiac dyspnea with diminishing cardiac reserve, the earliest symptom of a failing left ventricle, with pulmonary vascular congestion. The respiratory tract infection with cough is an added strain on the heart muscle. The paroxys-

mal dyspnea with substernal oppression was the most prominent symptom, more so than any crushing pain. It is the picture of cardiac asthma, of acute left ventricular failure; this is well known to be the conspicuous feature in some cases of proved coronary occlusion and myocardial infarction. Asthmatic rales were prominent, and interfered more, I gather, than the simple basal rales of congestive failure, with ascertaining whether the heart sounds were of good quality. It is important that no early diastolic blowing murmur of aortic regurgitation was audible. The blood pressure fell overnight. The next day the patient presented a picture of left-sided ventricular strain and failure, with little evidence of right-sided failure. The blood-pressure reading, which showed a lessened pulse pressure when he sat up, I take to be simply evidence of lessened ability of the circulatory apparatus to adapt to the change in position. This finding is observed in some hypertensive patients, but I think in this case is an indication of handicap in the circulatory apparatus. We have no evidence here for stating that the man had an antecedent hypertension. They have taken particular pains to tell us that during the acute episode the blood pressure was normal.

The fever on the day following the onset of symptoms, the rapid heart rate and the leukocytosis are all consistent with a diagnosis of myocardial infarction. The white-cell count is rather high, to be sure. The heart sounds were somewhat indistinct, in keeping with such a diagnosis. One wonders whether one could distinguish between a split second sound and gallop rhythm at the rate of 130. The electrocardiographic evidence of left bundle-branch block is consistent with the diagnosis of coronary occlusion. I believe this abnormal tracing sometimes occurs after an acute occlusion. On the other hand, it may indicate impoverishment of the blood supply of the heart muscle dating back over the months of exertional dyspnea; and the basis for such a process would be arteriosclerosis of the coronary arteries. The sedimentation rate I am inclined to discount as equivocal. The high red-cell count represents, I take it, a relative polycythemia due to the state of anoxemia, rather than being indicative of a true polycythemia.

Two questions arise as to differential diagnosis, the first as to whether this sudden accident and subsequent heart failure could be related to disease of the aorta. I think we can dismiss the possibility of a dissecting aneurysm because of the absence of outstanding pain with reference to the back and legs and the lack of a persisting hypertension. The question of a pulmonary embolus with acute cor pulmonale arises. I think the absence of any previous accident to the legs, however slight, the absence of edema of an ankle or any story of phlebitis and the absence of the characteristic evidence, however transient, which may by electrocardiogram be demonstrated after acute pulmonary emboli, are all points that would make us unable to entertain that diagnosis; however, it should be thought of — I think probably it was — in a man whose complaint was dyspnea and sternal oppression rather than pain.

Did syphilis play a part in this man's demise? He may well have had latent syphilitic aortitis, for such is not uncommonly the case, and perhaps one out of five individuals with latent syphilitic aortitis has no symptoms that would lead one to suspect the diagnosis. But I think two points are important: the paroxysmal dyspnea such as this man had is strikingly absent in uncomplicated syphilitic aortitis; and, although perhaps one out of six cases of syphilitic aortitis may have involvement of the coronary orifices in the process in the wall of the aorta, only about three fifths of these have symptoms of coronary insufficiency. I think it most unlikely then that, even if this man did have syphilitic aortitis, for which there was no time to be more certain by x-ray examination, his symptoms were due primarily to it, but rather to coronary disease with which the syphilis of the aorta was merely associated, if present at all. Myocardial infarction as a result of a syphilitic process that partially or completely blocks the orifices of a coronary artery is rare indeed, and among cases reported from the Presbyterian Hospital there were only three or four of this sort noted.[1]

The rare causes of relatively sudden cardiac death in cases with syphilis are probably not present here. Acute syphilitic myocarditis has been described but is still a point of controversy; and in such cases as I could find reported from the Baltimore City Hospital[2] about five years ago all were in younger individuals dying much more suddenly than this man who lived thirty-six hours after the first attack.

I should conclude that this man had, and that the pathologists would find, coronary thrombosis with myocardial infarction and possibly a syphilitic process at the root of the aorta, which one was unable to be more certain about during life.

Dr. J. H. Means: The first attack that he had sounds like a textbook description of acute pulmonary edema which might have been an occurrence not necessarily associated with coronary disease. I agree that the argument in favor of coronary oc-

clusion is very convincing. I should just like to mention that Dr. Mallory did an autopsy for me some years ago on a patient whose manner of exitus was very similar to that of this man, so far as I can judge it from the description just given, and found no thrombosis of the coronary arteries, no infarction, nothing but a narrow coronary, narrowed by an atheromatous process. So I just throw that out as a possibility in this man, not as a probability.

Dr. Tracy B. Mallory: Drs. Blumgart, Schlesinger and Davis,[3] as many of you undoubtedly know, have recently published a paper concerning the clinicopathological correlation of coronary artery disease and infarction of the myocardium in a considerable number of cases. They make a point with which I am very much in sympathy; namely, that the clinical diagnosis of coronary thrombosis is made very casually without realization that the syndrome is really that of infarction of the heart. Pure coronary thrombosis very frequently produces no recognizable clinical symptoms, and a diagnosis of coronary thrombosis does not necessarily connote infarction of the heart and vice versa. Dr. Baker has committed himself to both coronary thrombosis and myocardial infarction.

Dr. Paul D. White: I want to make a correction in the electrocardiographic interpretation. It should read right bundle-branch block rather than left. That brings up the possibility, as in a case discussed here a while ago, of widening of the QRS complex of the right bundle-branch type as due to cor pulmonale, a very unusual but interesting association. It is therefore conceivable, though not likely, that this patient had recurrent pulmonary infarction rather than massive myocardial change from coronary disease.

Dr. Means: If that is the case, pulmonary artery thrombosis becomes a possibility.

Clinical Diagnoses

Coronary heart disease.
Paroxysmal nocturnal dyspnea.

Dr. Baker's Diagnoses

Coronary thrombosis.
Myocardial infarction.
Syphilis of aorta?

Anatomical Diagnoses

Coronary sclerosis, severe.
Myocardial infarction, left ventricle.
Syphilitic aortitis with aneurysm.
Pulmonary edema and congestion.

Pathological Discussion

Dr. Mallory: The autopsy showed an enlarged heart, weighing 450 gm. There was massive infarction of almost the entire left ventricle, including the major part of the interventricular septum. The coronary arteries showed no demonstrable occlusion. They were everywhere markedly narrowed by atherosclerotic processes, and their mouths, particularly the mouth of the right coronary artery, were markedly narrowed by scars in the base of the aorta just above the aortic valve, which were undoubtedly syphilitic in origin. There was a very slight degree of separation of two of the aortic cusps. The conviction that this was a syphilitic process was raised to certainty when we found a small aneurysm at the beginning of the arch and a microscopic appearance entirely characteristic of syphilitic aortitis.

The lungs showed a very marked grade of pulmonary edema, and the other organs a slight amount of passive congestion, nothing else. So far as the autopsy was concerned I think we have good evidence of left-sided heart failure, and practically no evidence of right-sided failure.

Dr. Means: Since this man was Japanese, since we know diseases of this type vary from race to race, — we know, for instance, there is a difference between Negroes and Whites, — and since Dr. Cadbury, who is with us this morning, has just come back from Canton, I should like to ask him about coronary thrombosis and so forth in the Japanese. The Japanese now occupy Canton. Do they differ from our race with regard to cardiac symptomatology?

Dr. William W. Cadbury: I cannot speak for the Japanese. I see none of them. We send them to their own hospital. In the Chinese, coronary thrombosis is extremely rare.

Dr. Mallory: How about cardiovascular syphilis?

Dr. Cadbury: That is present. We get a fair amount of syphilitic disease of the aorta. Hypertension is relatively rare among the Chinese race.

References

1. Von Glahn, W. C.: Cardiovascular syphilis: pathology. *Nelson's Loose-Leaf Medicine*. Vol. 4. New York: Thomas Nelson & Sons, 1937. Pp. 341-362.
2. Magill, T. P.: Syphilitic myocarditis. *Bull. Johns Hopkins Hosp.* 57:22-31, 1935.
3. Blumgart, H. L.; Schlesinger, M. J., and Davis, D.: Studies on the relation of the clinical manifestations of angina pectoris, coronary thrombosis, and myocardial infarction to the pathologic findings. *Am. Heart J.* 19:1-91, 1940.

The New England
Journal of Medicine

Formerly the
Boston Medical and Surgical Journal

Established in 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Official Organ of
The Massachusetts Medical Society
The New Hampshire Medical Society
The Vermont State Medical Society

Editorial Board

Joseph Garland, M.D. — John P. Sutherland, M.D.
William B. Breed, M.D. — Stephen Rushmore, M.D.
George R. Minot, M.D. — Hans Zinsser, M.D.
Frank H. Lahey, M.D. — Henry R. Viets, M.D.
Shields Warren, M.D. — Robert M. Green, M.D.
George L. Tobey, Jr., M.D. — Charles C. Lund, M.D.
C. Guy Lane, M.D. — John F. Fulton, M.D.
William A. Rogers, M.D. — A. Warren Stearns, M.D.
Dwight O'Hara, M.D.

Associate Editors

Thomas H. Lanman, M.D. — Donald Munro, M.D.
Henry Jackson, Jr., M.D.

Walter P. Bowers, M.D., Editor Emeritus
Robert N. Nye, M.D., Managing Editor
Clara D. Davies, Assistant Editor

Subscription Terms: $6.00 per year in advance, postage paid, for the United States; Canada, $7.04 per year; $8.52 per year for all foreign countries belonging to the Postal Union.

Material for early publication should be received not later than noon on Saturday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

THE ANNUAL MEETING OF THE MASSACHUSETTS MEDICAL SOCIETY

For one hundred and fifty-nine years this oldest medical society, with a continuous existence in the United States, has conducted its annual sessions. The meeting this year was at the Copley-Plaza Hotel, Boston, May 21 and 22.

Every detail of the program, arranged by the committee in charge, was ready for the assemblage. After registration and study of the agenda, the fellows and guests devoted time to the scientific sessions, inspection of the scientific and commercial exhibits and conferences.

The total registration for the two days was 1461, but some of those present did not have their names recorded.

The round-table meetings and luncheons, arranged for the noon intermission of the main program on the first day, enabled the specialists to meet and discuss their particular problems without adjustment to the needs of a general audience. By this arrangement all fellows, except the councilors, could attend any scientific session without missing any subject on the program.

The attendance at the several meetings of the specialists was 89 for medicine, 70 for pediatrics, 144 for obstetrics, 50 for surgery and 50 for dermatology.

Twenty-two members competed for the award of the Burrage Bowl and other prizes, the winners being Oliver Lothrop, low net; J. W. Henderson, 2nd low net; Thomas Cavanaugh, 3rd low net; R. S. Nugent, low gross; Robert Dutton, 2nd low gross and Joel Melick, 3rd low gross.

Provision was made for the visiting ladies to play golf, sign up for treks to various places of interest and for dinner at Horticultural Hall followed by a Pop Concert. About two hundred visiting ladies registered, but the number participating in the special features of the program for them is not available.

Two hundred and twenty-eight attended the Tuesday-morning general clinical meeting. The Council meeting was in session at the same time, thereby affecting attendance. In the afternoon the number rose to 388, and, with the increased registration on Wednesday, the attendance at the morning clinical meeting was brought to over 400. In the afternoon the number reached at least 600, for many could not get into the hall. The attendance at the annual dinner on Tuesday evening was 264. The quality of this repast was unusually good and the social atmosphere was enjoyable.

The address of Thomas Parran, Surgeon General of the United States Public Health Service, in his delineation of the serious situation confronting the world and imposing great responsibilities on the people of this country, was a stirring appeal for united support of all classes. When, in closing, he portrayed the part medicine must play not only in meeting the peril to the health of the country but beyond that because of its understanding of the psychology of all classes and its opportunity for assuming leadership in maintaining the traditions and ideals of the preceding

years, he roused his audience to an outburst of applause which demonstrated his power to bring his hearers into harmony with his convictions.

The audience then adjourned to attend the Shattuck Lecture[1] in the adjacent hall, where 575 met to hear Dr. Ernest W. Goodpasture present a record of the efforts under way and the facts acquired in studies of the problems involved in virus infections and immunity relating thereto. His treatment of the complicated and abstruse subject of virus diseases was a demonstration of his ability to interest the average doctor and make clear the methods of approach to these problems.

A very large proportion of the 320 councilors were present at the meeting of that body, held on the forenoon of the first day. This is a demonstration of the interest shown by these officials in the affairs of the Society.

The first business on the program was the calling of the roll of the Nominating Committee with responses from delegates representing all but one of the eighteen district societies. The committee retired and soon returned, reporting a list of names for consideration of the Council, as follows: for president, Walter G. Phippen, of Salem; vice-president, Frank R. Ober, of Boston; secretary, Alexander S. Begg, of West Roxbury; treasurer, Charles S. Butler, of Boston; and orator, A. Warren Stearns, of Billerica. No other nominations appearing, the recommendations of the committee were approved and the Council unanimously elected the persons named for the respective offices.

Most of the time was given to consideration of the reports of the standing and other committees. So much study had been given to the duties of these committees and so much care in the drafting of their reports that they were accepted and the several recommendations adopted with only minor amendments in few instances and with no extended discussion.

The President's nomination for membership of committees was submitted and adopted without debate. No incidental business having been proposed, the meeting was dissolved after being in session less than an hour and a half; it was generally regarded as one of the shortest Council meetings of many years. The official record will be published in the June 20 issue of the *Journal* and should be studied by the fellows of the Society for, according to certain recommendations, changes in the by-laws, as suggested by the Committee on Medical Education and Medical Diplomas, should have study by the general membership.

The annual business meeting of the Society, with the President's address and the Annual Discourse, was called to order by the President at eleven o'clock Wednesday morning. The first business was the report of the Secretary, showing that the losses to the membership consisted of 99 deaths, 23 resignations and 38 deprivations, making a total of 160. The additions consisted of 252 new members with 3 readmissions and 10 restorations, a total of 265, making a net gain of 105, bringing the membership to 5542.

No item of business appearing, the President then delivered the annual report on the condition of the Society, which he described as "very healthy" and after paying tributes to the Secretary, Treasurer, the councilors, committee members and all who have assisted in the administration of the affairs of the organization, he appealed for a concerted effort to induce all worthy physicians of this State to become members of the Society.

He then explained the methods adopted for conducting the affairs of the American Medical Association and the relation of this Society thereto. Other subjects presented were the advisability of more general utilization of the clinical material of the many hospitals in the State for postgraduate education, careful financial planning of the activities of the Society, and maintenance of the traditions and high principles of the profession so that the pitfalls into which some societies have fallen may be avoided. This address and others delivered at the meeting will be published in early issues of the *Journal*.

The Annual Discourse by Dr. William Jason Mixter on "New England, Neurosurgery and the Neurosurgeon" was then delivered.[2] This essay will take high rank among others delivered before the Society.

The meeting then adjourned for luncheon, furnished by the Society, with 327 members participating.

The general arrangements for the meeting were frequently commended by those in attendance with approval of the work of the Committee of Arrangements and the hope that subsequent meetings will follow the general scheme of this year. The only dissatisfaction expressed was that for a society of this size and with a very attractive program for its annual meeting, the attendance seemed to indicate that the large number of absentees do not appreciate the advantages of attending these meetings. However that may be, it is certain that those who were present profited by the experience.

REFERENCES

1. Goodpasture, E. W.: Immunity to virus diseases: some theoretical and practical considerations. *New Eng. J. Med.* 222:901-910, 1940.
2. Mixter, W. J.: New England, neurosurgery and the neurosurgeon. *New Eng. J. Med.* 222:865-869, 1940.

TWENTY-FIRST ANNUAL REPORT OF THE COMMONWEALTH FUND

On October 17, 1918, the Commonwealth Fund was established by Mrs. Stephen Harkness with the avowed purpose of applying the resources of this trust to "promote the welfare of mankind." Every year since that time a report giving the details of the activities carried on by the administrative staff and the five main divisions, including the committees appointed for specified functions and the Child Guidance Council of Great Britain, has been published. These documents have demonstrated a broad conception of methods that may be employed to meet the problems relating to medicine, public health, and economic and sociologic conditions of the human race. It is probably true that the inciting reason for the establishment of this fund in 1918 was the chaotic situation incident to the war at that time, and although for several years grants from the fund were provided to help in the rehabilitation of the social structure, as time went on its interests became especially concentrated in the promotion of American health and agencies connected with progress in this direction. These yearly reports show the accomplishments of this organization and demonstrate the wisdom of the plans adopted and the executive ability exercised in their application.

During the twenty-one years of operation nearly $24,000,000 have been distributed to hospitals, state health departments, medical schools, clinics and medical societies. One interesting movement has been that of financing studies relating to criminology and various forms of social service, apparently in furtherance of the plan to bring preventive measures to bear on delinquency, which is possibly a factor in establishing anti-social tendencies.

Fortunately the educational features of this report are not obscured by dry statistical tables, but are presented in an engaging fashion which carries assurance of the generous concern of the officials of the Commonwealth Fund in the problems of human welfare. The report is worthy of careful study because of its informative quality; it will interest every student of the problems of medical education and public-health administration.

MEDICAL EPONYM

Buerger's Disease

Leo Buerger's (1879–) description of the disease bearing his name first appeared in the *American Journal of the Medical Sciences* (N. S. 136:567–580, 1908), under the title "Thromboangiitis Obliterans: A study of the vascular lesions leading to presenile spontaneous gangrene."

> The disease occurs frequently, although not exclusively, among the Polish and Russian Jews. . . . We usually find it occurring in young adults. . . . After longer or shorter periods, characterized by pain, coldness of the feet, ischemia, intermittent claudication, and erythromelalgic symptoms, evidences of trophic disturbances appear which finally pass over into a condition of dry gangrene. . . . I . . . have come to the conclusion that we are dealing here with a thrombotic process in the arteries and veins followed by organization and canalization, and not with an obliterating endarteritis. . . . I would suggest that the names *"endarteritis obliterans"* and *"arteriosclerotic gangrene"* be discarded in this connection, and that we adopt the terms *"obliterating thrombo-angiitis" of the lower extremities* when we wish to speak of the disease under discussion.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

PYELITIS OF PREGNANCY TREATED BY NEPHROSTOMY

Mrs. E. L. F., a twenty-five-year-old primipara, five and a half months' pregnant, was admitted to the hospital on February 19, 1932, complaining of pain in the right groin with chills and fever of five days' duration. Shortly before there had been a milder attack with pain on the left side.

The family history was irrelevant. She had had no miscarriages and no children. An appendectomy had been performed four years previously. Catamenia had always been regular with a twenty-eight-day cycle and lasted three to four days without dysmenorrhea. The last regular period had occurred on September 17, 1931, making the expected date of confinement June 24.

Physical examination revealed a well-developed and fairly well-nourished young woman who presented the appearance of serious illness. The temperature on the evening of admission was 99.4°F., the pulse 124, and the respirations 28. The following morning the temperature was 102°F., the pulse 120, the respirations 24, and the blood pressure 95 systolic, 65 diastolic. The fundus of the uterus was at the level of the umbilicus. There was slight tenderness but no spasm in the right lower quadrant. Extreme tenderness and some muscle resistance were found in the right lumbar region. The entire abdomen was markedly distended, and the flanks were faintly edematous. A catheter specimen of urine contained innumerable pus cells in large clumps. The white-cell count was 9800. On the day after entry the patient developed a generalized punctate rash, which a medical consultant believed to be the result of toxemia.

On February 23, four days after admission, and when an intensive medical program had failed to afford relief, cystoscopic examination was carried out. The pelvis of the right kidney was irrigated with boric acid solution, followed by the introduction of 10 cc. of 2 per cent Mercurochrome. The catheter was left in position in the right ureter for twenty-four hours. The white-cell count at this time was 22,000. The blood urea-nitrogen was 25.6 mg. per 100 cc. The blood Wassermann was negative. Urine obtained from the right kidney was thick and purulent, and the sediment contained 30 or 40 pus cells per high-power field; the culture showed colon bacilli.

Three days later, on February 26, the temperature was subnormal and the pulse 120. The patient seemed somewhat improved, but the right kidney was still large and tender. Antiseptic lavage of the right renal pelvis was repeated, and a ureteral catheter again left in situ. The urine from this kidney appeared to be less cloudy but still contained abundant pus. Two days later the temperature and pulse rate had begun to subside but abdominal distention persisted. There was a mass in the right lumbar region which seemed to be increasing in size, and the patient was definitely jaundiced. It was decided to do a right nephrostomy.

The operation was performed on March 1 under nitrous oxide, oxygen and ether anesthesia, with the evacuation of a large amount of thick pus from the renal pelvis. Convalescence from the operation was perfectly satisfactory, except that the blood showed a hemoglobin of 55 per cent, a red-cell count of 3,850,000 and a white-cell count of 18,000. Because of this, 400 cc. of citrated blood was given by transfusion on March 8. The patient suffered an attack of mastoiditis two days later, which was treated conservatively. On April 1 perirectal abscesses developed; these were satisfactorily treated by poultices.

On April 16 the patient was delivered by low forceps of a premature child, who was in good condition. The patient was discharged on May 2. There is no follow-up record on this patient.

Comment. This is a most unusual and severe case of pyelitis during pregnancy, complicated by mastoiditis. Conservative medical treatment, renal lavage and ureteral catheterization failing, nephrostomy was performed with highly satisfactory results. This procedure is rarely necessary, and then only as a life-saving measure.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

DEATHS

BENNER — BURNHAM R. BENNER, M.D., of Lowell, died May 29. He was in his ninety-fourth year.

Born in Pittston, Maine, he received his education in the public schools of Roxbury and the Harvard Medical School, receiving his degree from Columbia University College of Physicians and Surgeons, New York City, in 1875.

Dr. Benner was a member of the Massachusetts Medical Society and the American Medical Association, and had retired from active practice.

GOODMAN — SAMUEL GOODMAN, M.D., of Boston, died May 28. He was in his seventy-sixth year.

Born in Kalwarya, Lithuania, he came to New York City in 1871. He received his degree from New York University Medical College in 1889 and began the practice of medicine in Boston the following year. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a son and a daughter, survive him.

SEARS — GEORGE G. SEARS, M.D., of Boston, died May 27. He was in his eighty-second year.

Dr. Sears attended Amherst College and received his degree from the Harvard Medical School in 1885. He was former chief of the medical staff and trustee of the Boston City Hospital, and was instrumental in founding the Thorndike Memorial Laboratory at the Boston City Hospital. Since 1924 he was a trustee of the Forsyth Dental Infirmary and was professor emeritus of clinical medicine at Harvard Medical School.

Dr. Sears was a member of the Massachusetts Medical Society, the American Medical Association and the Association of American Physicians.

A daughter and two grandchildren survive him.

222
40

CORRESPONDENCE

A WARNING

To the Members of the Massachusetts Medical Society:

A man giving the name of Roger Maloney and stating that he was engaged in the cancer education program called on a fellow of the Society, April 16, at 9 p.m., claiming that he was stranded and needed a loan of three or four dollars. He gave my name as reference.

No one is employed by the Cancer Committee of the Massachusetts Medical Society or authorized to ask for funds.

SHIELDS WARREN, M.D., *Chairman,*
Cancer Committee.

195 Pilgrim Road,
Boston.

ASSOCIATED HOSPITAL SERVICE

To the Members of the Massachusetts Medical Society:

We have moved to larger quarters. Our new location is the Western Union Building, 230 Congress Street. Our telephone number is Hubbard 8800.

We appreciate the fact that the unusual growth of the Blue Cross, which made this move necessary within two and a half years, is due largely to your acceptance and endorsement of our place in the hospital work of the community.

Three thousand two hundred and eighteen doctors have sent 38,000 Blue Cross patients to Massachusetts hospitals during the past two and a half years. With rare exception you have graciously co-operated with us in making fair decisions in connection with these admissions. Because we believe that 95 per cent of you are interested in the continued success of the Blue Cross, we do not hesitate to lay before you one of our current problems.

We have observed the tendency of our subscribers to stay in the hospital as long as Blue Cross benefits are available. This indicates that the length of stay is very often governed by these benefits and not by the course of the patient's illness. We shall never attempt to decide here how long a patient should be hospitalized for a given illness. We know that treatment is not a matter of statistics.

The solution to this problem is to reach the subscriber with an appeal for fair play and to educate him in the fact that his full benefits are available only if needed, but that abuse of these benefits could result in a general loss to all subscribers.

To this end we earnestly request your support.

R. F. CAHALANE, *Executive Director.*

230 Congress Street,
Boston.

REPORTS OF MEETINGS

BOSTON ORTHOPEDIC CLUB

At a meeting of the Boston Orthopedic Club at the Boston Medical Library on February 12, Dr. Bernard M. Jacobson spoke on "The Diagnosis of Multiple Myeloma," describing studies by himself and Drs. Alfred Kranes, Edward A. Gall and James R. Lingley. The speaker briefly recounted the previous eras in the diagnosis of this disease, the first prior to 1898 when the appearance of one or more visible tumors was the only method available, and the second from 1898 to 1933, when the condition was suspected only on roentgenological findings.

That multiple myeloma is actually increasing was demonstrated both by the percentage of admissions and by that of autopsies for successive periods. From 1913 to 1917 there were at the Massachusetts General Hospital 0.3 cases per 10,000 admissions, and this increased to 3.5 cases from 1933 to 1937. That better diagnosis did not account for this rise was shown by the post-mortem statistics, which showed that there have been 6 cases of multiple myeloma in every 1000 autopsies since 1933, as compared with 1 case prior to that date. No cases have been solicited, Dr. Jacobson pointed out. The modern era in the diagnosis of multiple myeloma, which started at the Massachusetts General Hospital in 1933, includes 29 cases, which served as a basis for Dr. Jacobson's talk.

The outstanding symptom was pain in 21 of the patients, in 9 of whom it simulated polyarthritis. Pain in the spine or hips, which is emphasized in textbooks, was found in only 8, and pleuritic pain predominated in 6 patients. Physical examination was not found very useful, for only 11 of 28 showed abnormal signs. Five of these were in the spine, 4 in peripheral joints and 2 in the ribs.

It was in regard to laboratory data that Dr. Jacobson found the greatest diagnostic assistance. Presumptive findings were Bence-Jones proteinuria, which occurred in half the cases, and plasma cells in the blood smear, which were found in 20 per cent. Considered strongly suggestive evidence were "typical" roentgenological findings (40 per cent), a plasma protein value of more than 8 gm. per 100 cc. (50 per cent) and an elevated blood calcium in the presence of a normal phosphatase (40 per cent). Somewhat less suggestive tests were the characteristic precipitation of Hayem's solution (50 per cent), an anemia which tended to be macrocytic (90 per cent) and renal insufficiency (40 per cent).

The speaker then discussed each of these diagnostic aids in detail. The only diagnostic roentgenologic changes were described as small, fairly discrete areas of decreased density found most frequently diffusely distributed, in the skull (in 10 of 25 cases), pelvis (in 6 of 21 cases), spine (in 5 of 21 cases) and ribs (in 3 of 23 cases). This was found not to be a true index of the degree of bone-marrow invasion, however, for the last x-ray films were

often negative even when the autopsy showed bone lesions. The differential diagnosis should include metastatic carcinoma, hyperparathyroidism, senile osteoporosis, Paget's disease and giant-cell tumor. It was suggested that if only one plate can be obtained that of the skull is most apt to be helpful.

Dr. Jacobson stressed the importance of an elevated serum protein, which was found to depend on an increase of the globulin fraction. A total protein of more than 8 gm. per 100 cc. was found in 14 of 26 cases, while a globulin value above 3 gm. was present in all 13 patients in whom the determination was made. The formol-gel test, which depends on this latter phenomenon, was found positive in each of the 10 cases in which it was tried, and was advocated as the earliest and easiest means of determining the presence of this highly suggestive elevation of globulin. The precipitation of Hayem's solution during a routine blood count, which was noted in almost half the cases, was also attributed to this alteration in the blood.

Hypercalcemia of 11 to 14 mg. per 100 cc. was observed in 9 of 22 patients, whereas the serum phosphatase had a value of less than 5 Bodansky units in 17 of these cases. This combination of circumstances, together with a serum phosphorus of 3 to 5 mg. per 100 cc. found in 18 of 23 cases, helped in ruling out hyperparathyroidism, Paget's disease and most cases of metastatic carcinoma.

Renal insufficiency, evidenced by an elevated nonprotein nitrogen and a diminished phenolsulfonephthalein excretion in 13 of 29 patients, was considered to be caused by the amorphous precipitate found in the kidneys and identified as Bence-Jones protein. The condition was described as a "tubular hydronephrosis." Terminal uremia ensued in 7 of 15 patients examined, and 10 of these exhibited pathological evidence of renal involvement.

Dr. Jacobson pointed out that 24 of 29 patients were suspected of having multiple myeloma before biopsy or autopsy, as a result of following up an initial clue. This clue in 10 of 29 cases was offered by the roentgenograms either alone or together with a urinalysis or a renal function test. Anemia, usually with x-ray or blood chemical findings, showed the way in 6 cases, while altered blood chemical findings and the presence of plasma cells in the routine blood smear offered the initial clue in 4 or 5 cases each.

It was instructive that only 6 of 29 patients were x-rayed because of symptoms — 5 for back or hip pain and 1 for rib pain. Two cases were primarily considered to be due to pulmonary carcinoma and pleurisy respectively.

The diagnosis, Dr. Jacobson pointed out, must be substantiated by histological examination. Biopsy sites suggested were accessible lesions, or cancellous marrow, such as that of the sternum studied by means of a sternal puncture. The latter established the diagnosis in 8 of 29 cases.

The prognosis was held to be grave. In 17 of the 20 fatal cases the patients died in one to sixteen months, with an average of seven months, while in 3 they lived two to three and a half years. One patient is living after five years, having had a peripheral lymph node positively diagnosed, but having as yet no demonstrable bone lesions by x-ray. Deep x-ray therapy, both local and spray, was found useless in prolonging life, and only of questionable value for the relief of spinal pain.

In discussion Dr. George W. Holmes admitted that the skull offers the best single chance of finding bone lesions by x-ray but warned that lesions may occur elsewhere when the skull appears negative. He pointed out that roentgenological evidence is present only after involvement of the cortex, which may occur late or never in a condition affecting primarily the marrow.

Dr. Benjamin Castleman emphasized the importance of the technic of determining Bence-Jones proteinuria. He said that solitary myeloma, although possible, is usually indicative of an early case or a single manifestation of an already widespread condition. Pathologically, splenomegaly was found in half the cases — a compensatory hematopoiesis for the decreased amount of bone marrow. The finding of a more or less normal phosphatase value was explained by the nature of the process, which is almost entirely destructive rather than formative.

Dr. Jacobson concluded with the statement that the cancellous bone is invaded 100 per cent, despite negative x-ray evidence or gross autopsy examination. Patients with a "solitary plasmoma" have lived eight to ten years, but their span is usually two to three years, postmortem examinations reveal widespread disease and even early sternal biopsy is usually positive.

HARVARD MEDICAL SOCIETY

A regular meeting of the Harvard Medical Society was held at the Peter Bent Brigham Hospital on February 27, with Dr. Frank R. Ober presiding.

There was the usual presentation of cases. The medical patient was a twenty-three-year-old girl admitted with a complaint of external dyspnea for one year and a chronic cough for six months. As a child, she had been admitted to the Children's Hospital complaining of nausea, vomiting, and stiff neck. The spinal fluid contained 5 monocytes per cubic millimeter; there was an anemia and clumps of leukocytes were found in the urine. She was discharged well but returned in two months with a positive Kernig sign, increased spinal-fluid pressure and an elevated globulin content. A diagnosis of acute anterior poliomyelitis was made, and corrective operations were performed later. There were always clumps of white blood cells in the urine at subsequent admissions. The patient, being able to get around on crutches, had worked until one week prior to the present admission. Digitalis had been recommended six months before by a local doctor but was voluntarily discontinued in October. Physical examination revealed an enlarged heart with a presystolic gallop rhythm, basal rales in the lungs, weakness of the arms and a deformed left leg. The hemoglobin was 24 per cent, the erythrocyte count 1,400,000, and the leukocytes 6000. The serum calcium was 8.8 mg. and the phosphorus 11.0 mg. per 100 cc., and there was a reversed albumin-globulin ratio. Roentgenograms demonstrated an enlarged heart, congestive lung changes, marked atrophy of the left leg and odd changes of the vertebrae. A blood transfusion was administered after an attempt to improve the patient's general condition, but there resulted temporary orthopnea. While in the hospital there was an episode of eight convulsions which finally responded to chloroform after intravenous calcium lactate and the barbiturates had failed.

Dr. M. C. Sosman stated that the appearance of dense vertebral plates was disturbing when one was looking for evidences of renal rickets. In that condition one expects true decalcification rather than ossification. Dr. Soma Weiss remarked that the congestive failure was undoubtedly secondary to a chronic pyelonephritis dating from childhood although unsupported by a positive history. He noted the presence of left-sided heart failure, as evidenced by the x-ray films and by clinical manifestations, and the absence of right-sided failure, a combination which caused orthopnea only after a transfusion, and said that anemia

might explain this phenomenon. Dr. Weiss added that bone changes are a common accompaniment of pyelonephritis occurring in childhood and may cause physical retardation and renal dwarfism.

The surgical case was that of a fourteen-year-old boy who was one of twins born at a difficult birth and who had had an illness at two years of age which was possibly poliomyelitis. Following that episode there was gradual difficulty in touching his left heel to the ground. Athetosis of the left arm developed at the age of nine, and a chordotomy for postencephalitic athetosis was performed three years later at another hospital. Somewhat later there intervened episodes of falling backward; his head was held to the right with hypertrophy of the neck muscles, and there was weakness of the muscles on the left with spasticity of the leg on that side.

In discussing the case, Dr. Ober reminded his audience that spastic and flaccid paralyses occurring in the same patient are rare. Nature does not seem to strengthen the limbs of the poliomyelitis victim by superimposing a spastic paralysis. Dr. William T. Green stated that this boy had had his athetosis well cared for, but that follow-ups on this and other cases indicate that there may be a progressive muscle weakness on the affected side and possibly a recurrence of the athetosis.

The speaker of the evening was Dr. Ralph K. Ghormley, of Rochester, Minnesota, whose subject was "The Life History of Bone Grafts: Experimental and clinical observations." Dr. Ghormley stated that his concept that the effectiveness of the take of a graft was proportional to its permeability resulted originally from some observations on patients decalcified and subjected to straightening of their scolioses by Dr. J. C. Aub.

The speed of take was determined for various bone grafts in adult dogs. Periosteal grafts showed no activity, and it was concluded that this layer of bone acts merely as a limiting membrane in the adult. Cortical grafts resulted only in preosseous tissue being laid down, whereas cancellous bone removed from the iliac crest showed rapid invasion by the host. It was pointed out that these transplants atrophy to some extent over a period of time and are subject to fractures during this temporary weakness. Dr. Ghormley stated that the mechanism is one of metaplasia of the surrounding tissue and that chemistry and the porosity of the graft are important factors in the efficacy of the operation.

The speaker went on to describe the optimal graft for various sites. Cortical bone, especially from the tibia, was advocated for splinting of ununited long-bone fractures, scoliosis, large cystic defects, tuberculous spondylitis and spondylolisthesis. Cancellous grafts, preferably from the iliac crest, were considered suitable for lumbosacral stabilization of two vertebrae only, for shelving operations in old congenital dislocation of the hip, for filling large bone cysts in combination with cortical bone and for ankylosing a hip. Osteoperiosteal grafts were held useful only in extensive scoliosis of the spinal column where the curve prevents the use of more stable transplants. The fibula, due to its resistance to a shearing force, can be used to advantage for ununited fractures of the femoral neck and for replacement of the tibia in the Huntington operation. Rib grafts may be employed, suggested Dr. Ghormley, where scoliosis, causing severe rib deformity, makes it advisable to remove ribs and replace them along the spinal column. The chip and shave grafts were called risky due to their tendency to resorb readily, especially in the presence of even slight infection. Match grafts, which are merely special-shaped cortical bone, were deemed satisfactory for uniting bone. "Delayed" grafts, which are left in the donor temporarily after cutting, were held to be merely another method for obtaining optimal permeability of the bone transplant.

Dr. Ghormley, in considering homogeneous grafts, concluded that they give less satisfactory results than autogenous ones and that the closeness of kin has no effect on the results. He was of the opinion that it is wise to match the serums preoperatively even though this has not been proved necessary. Heterogeneous grafts should be used only in those circumstances in which autogenous or homogenous grafts are not available.

Infection was said to be the commonest complication of bone grafting. Dr. Ghormley recommended waiting six months to two years after the primary infection has apparently subsided before attempting such procedures. When this complication appears after grafting, conservative treatment of the wound often leads to an ultimately good result. It was stated that the most important factor is the amount of resultant scar tissue around and between the bone fragments. Fracture may occur in the graft on malunited or ununited fractures and these should be immobilized by external fixation. Such complicating fractures may reunite in cases of scoliosis but not of tuberculosis of the spinal column.

The course of such transplants depends on the amount of invasion by the surrounding connective tissue. Usually the grafts remain in situ and are incorporated in the host bone as a result of the activity from stress and strain on the weakened part. The character of the engrafted bone remains unchanged. Grafts may occasionally be entirely absorbed for unknown reasons.

Dr. Robert Osgood, during the discussion, questioned whether the status of the osteoperiosteal graft had been decided in regard to its osteogenesis. He stated that it depended on one's concept of what constitutes the periosteum and consequently how much is removed. Dr. Ghormley agreed and emphasized that the degree of osteogenesis is also inversely proportional to the age of the donor.

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The regular meeting of the New England Society of Physical Medicine, held at the Hotel Kenmore on February 28, was devoted to a symposium on the treatment of arthritis. The internal aspects of the subject were discussed by Dr. J. Sydney Stillman. He considered the arthritides in two groups, one in which the etiology was known, the other in which it was unknown; he emphasized that it was in the former group that the internist procured the best results. The striking results in the management of gonococcal arthritis with sulfanilamide and the promising results of sulfathiozol in the treatment of staphylococcal infections were mentioned. Colchicine, instead of cinchophen, was recommended for gout, since adequate relief of pain can be gained without the danger of marked toxicity.

In the treatment of arthritis of unknown cause, Dr. Stillman reminded the group of the lack of a measuring stick for the evaluation of various measures. However, it was believed at the Robert Breck Brigham Hospital that examination of the hemoglobin, the sedimentation index, the weight of the patient and the local condition of the joints offered the best criteria for evaluation. Removal of the foci of infection was considered no more beneficial in patients with arthritis than in others, and it was ad-

vocated only in cases where such a procedure would ordinarily be carried out. The anemia, which is often resistant, should be attacked by transfusions. The vitamins were found not to benefit the arthritis, even when known deficiencies were corrected. Psychotherapy was stressed as a valuable adjunct to therapy since studies have shown that in the majority of patients with rheumatoid arthritis the onset of the disease or the exacerbations are related to emotional or economic stress. Estrin may benefit a certain number of women with menopausal arthralgia if given in doses of 10,000 to 30,000 units weekly, it was stated. Bee-sting, snake venom, artificial jaundice and sulfur were held to be unsatisfactory forms of treatment, while gold injections were considered too dangerous for the questionable benefit obtained.

Dr. J. P. Bill discussed "Diet and Hygiene for the Arthritic." The speaker impressed on this audience the importance of proper clothing, heating and well-rounded diets amid cheery surroundings. Dr. Bill was of the opinion that foci of infection should be diligently searched for and attacked, and that the colon was undoubtedly an underestimated source of such trouble. The manufacture of simple apparatus for applying dry heat and contrast baths in the home was described, and this type of treatment was advocated for the large group of patients who are unable to afford the orthodox methods. Dr. Bill suggested a diet individualized with due regard to the idiosyncrasies of the patient and his need for added or decreased weight.

"The Use and Abuse of Physical Agents" was the title of the talk by Dr. Herman A. Osgood. He listed among abuses the employment of complicated methods when simpler measures are adequate, the overemphasis of one form of treatment or type of apparatus and the use of uncomfortable and even dangerous fever therapy when unnecessary. The preliminary use of heat prior to massage was advocated, with the infra-red lamp being used for superficial heat and diathermy for deep heat. It was pointed out that short-wave diathermy is merely a convenient form of heat and has no therapeutic specificity. Overheating may injure the cartilage if prolonged. X-ray therapy may prove beneficial in rheumatoid arthritis, may relieve pain in hypertrophic arthritis and may depress the overgrowth of pannus by its action on the sensitive young cells.

The final talk of the evening, on the orthopedic aspects of the problem, was presented by Dr. Loring T. Swaim. The importance of proper posture as a protective measure for the proper functioning of vital organs was stressed. Recent work has shown the value of preventing rather than attempting to treat deformities of arthritis. During the acute, painful stage, plaster shells are applied to the affected part in the most comfortable approach to an overcorrection of the tendency to flexion deformities. It was found that this allows complete muscular relaxation and prevents the damaging spasm.

The striking results of these measures were demonstrated in Strümpell-Marie's disease, where jackets are applied to prevent and help correct the "poker-back." Fifty per cent of an original group were found to have complicating fixation of the hips, and half of these were greatly benefited by this plaster jacket. During a five-year period, no patient treated early in the disease by this method has developed ankylosis of the hips; Dr. Swaim suggested that such changes are secondary to the spine deformity. It was even claimed that some slight improvement may be brought about in already fused spines by gradual straightening of the jacket, while progression of ankylosis can certainly be retarded if not prevented.

NOTICE

ANNOUNCEMENT

SYDNEY J. ALLMAN, M.D., announces that his correct address is 52 Columbia Road, Dorchester, and not 215 Main Street, Hightstown, New Jersey, as given in the *Directory of the Officers and Fellows* of the Massachusetts Medical Society.

SOCIETY MEETINGS AND CONFERENCES

JUNE 7, 8 — American Heart Association. Page 469, issue of March 14.

JUNE 7–10 — American Board of Obstetrics and Gynecology. Page 608, issue of April 4.

JUNE 8 — Dedication of Osler Memorial. Page 862, issue of May 16.

JUNE 8 and 10 — American Board of Ophthalmology. Page 719, issue of November 2.

JUNE 8–10 — American College of Chest Physicians. Page 781, issue of May 2.

JUNE 10 — American Medical Golfing Association. Page 824, issue of May 9.

JUNE 10, 11 — American Neisserian Medical Society. Page 898, issue of May 23.

JUNE 10–14 — American Medical Association. Annual meeting, New York City.

JUNE 10–14 — American Physicians' Art Association. Page 332, issue of February 22.

JUNE 12 — Harvard Medical Alumni Association. Page 938, issue of May 30.

JUNE 12 — New England Obstetrical and Gynecological Society. Page 898, issue of May 23.

JUNE 12 — Jefferson Medical College Alumni Association. Page 898, issue of May 23.

JUNE 23–25 — Maine Medical Association. Annual meeting. Rangeley Lakes.

JUNE 25–27 — Medical Library Association. Page 862, issue of May 16.

JUNE 27 — Pentucket Association of Physicians. The Try-Angle, Groveland.

SEPTEMBER 2–6 — American Congress of Physical Therapy. Page 862, issue of May 16.

OCTOBER 8–11 — American Public Health Association. Page 655, issue of April 11.

OCTOBER 11, 12 — Pan-American Congress of Ophthalmology. Page 898, issue of May 23.

OCTOBER 14–25 — 1940 Graduate Fortnight of the New York Academy of Medicine. Page 938, issue of May 30.

OCTOBER 21 — American Board of Internal Medicine, Inc. Page 369, issue of February 29.

DISTRICT MEDICAL SOCIETY

MIDDLESEX NORTH

JULY 31.

OCTOBER 30.

BOOK REVIEWS

Gonorrhea in the Male and Female: A book for practitioners. P. S. Pelouze. Third edition, thoroughly revised. 489 pp. Philadelphia and London: W. B. Saunders Co., 1939. $6.00.

This book has become established as the American classic on the subject, and consequently a third edition is welcomed, especially as it appears at a time when such drugs as sulfanilamide and sulfapyridine have come into widespread use in the treatment of gonorrhea. Dr. Pelouze warns against too ready belief that the disease has been completely eradicated; he cites cases in which the disease recurred soon after a quick sulfanilamide "cure," and advises continuing to use the time-tried proofs-of-cure before pronouncing a patient well.

In addition to urethritis and endocervicitis, Dr. Pelouze goes into the various complications of gonorrhea, such as arthritis, proctitis and so forth. The section containing case histories has been omitted, but Dr. Pelouze,

who is a crusader for the better control of gonorrhea and for the abolition of the taboos surrounding the whole subject, has added one on "The Medical Profession and Gonorrhea Control."

All in all, this new edition, which goes thoroughly and fundamentally into all aspects, both scientific and social, of gonorrhea, will undoubtedly ensure the continuance of this book's pre-eminent position.

Traitement de la Blennorragie par le sulfamide, une sulfone et leurs dérivés. M. Palazzoli and F. Nitti. 195 pp. Paris: Masson et Cie, 1939. 35 Fr. fr.

Specific chemotherapy has radically changed the treatment of gonorrhea. Sulfanilamide was first used for this purpose in 1937, with results which were truly amazing. Other sulfur compounds, derivatives of sulfanilamide and developed for the most part in Europe, have been employed for this purpose. The authors of this monograph write from extensive experience in the research laboratories and clinics of the Institut Pasteur and Institut Prophylactique and Hôpital Broca of Paris. A review of former methods of treating gonorrhea, admittedly ineffective, is contrasted with the brilliant results now obtained when the sulfur compounds are properly used. The action, dosage and results obtained with sulfanilamide and four of its derivatives are discussed in a convincing manner. Sulfapyridine and para-amino-benzene-acetyl-sulfamide are preferred to other compounds. The small doses of all these drugs as used by the authors are of considerable interest and raise the question as to whether therapy has not been too enthusiastic in this country. This book is easily read with a minimum knowledge of French, and should be studied by anybody interested in the treatment of gonorrhea.

The Employment of Fine Silk in Preference to Catgut: The advantages of transfixing tissues and vessels in controlling haemorrhage. William S. Halsted. 34 pp. Boston: Welch Bibliophilic Society, 1939. $3.00.

Shortly before his death, Dr. William H. Welch suggested to a group of his friends that a small society be founded for the purpose of republishing medical papers and treatises of importance which were not easily available to the student or scholar. At intervals since then, the Welch Bibliophilic Society has caused to be reprinted such papers as Welch's own remarkable monograph "The Interdependence of Medicine with Other Sciences of Nature" and Holmes's "Dissertation on Acute Pericarditis."

The present publication would have delighted the society's patron. It is in many respects the most important of his great friend Halsted's publications. In it are clearly and characteristically set forth the great principles of America's greatest surgeon, namely absolute hemostasis, delicacy in the manipulation of tissues and the leaving of a minimal amount of the least irritating foreign material in the wound; also included is an account of the first use of rubber gloves, gutta-percha tissue and silver foil. The exposition is based on the advantages of fine silk as a suture material, for its use enforces a discipline on the surgeon which makes roughness and careless hemostasis impossible. The reappearance of this paper is timely, in view of the vindication which Halsted's teachings are receiving from the clinical and laboratory researches of Reid, Whipple, Parsons, Shambaugh and Dunphy and many others.

The volume, like its predecessors, is a triumph of the bookmaker's art. The paper, typography and binding are beautiful; the reproductions of Brodel's unique illustrations are excellent. It will be eagerly sought by libraries, collectors and surgeons, since the edition is limited. The reviewer is amazed at the modest price for which the book is offered. It is to be hoped that reprintings of the first edition can be arranged so that it will become easily available to senior students and interns in surgery, for whom it should be required reading.

Medical State Board Examinations: Topical summaries and answers. An organized review of actual questions given in medical licensing examinations throughout the United States. Harold Rypins. Fourth edition, revised. 448 pp. Philadelphia, Montreal and London: J. B. Lippincott Co., 1939. $4.50.

This book was designed to assist graduates of approved medical schools to pass examinations conducted by the medical registration boards of this country.

The late author had had a long experience on these boards and also on the faculties of medical schools and was therefore qualified to approach the problems of medical education and licensure with an understanding mind. He found that some applicants for medical registration appear before examining boards handicapped by the disturbing fear of failure or in poor physical or mental condition because of faulty preparation for the ordeal.

Even though the rejection of graduates of approved medical schools does not exceed 5 per cent on the average, some worthy candidates need advice as to the best ways to prepare for the examination and the art of expression in order to satisfy the authorities of competence necessary to meet the exigencies of medical practice.

It is well explained in the text that the custom of so-called cramming and the use of stimulants immediately before an examination tend to upset the mental equilibrium of a candidate and that this may operate to his disadvantage. Another warning is expressed in the explanation that the written question and answer method does not cover the scope of the examinations as now conducted by many boards, for the candidate may be required to show familiarity with technical laboratory methods which are not susceptible of written descriptions.

Taken all together the applicant for medical licensure may study this book and profit by the advice contained therein. It is well written and informative to an unusual degree.

Treatment in General Practice: The management of some major medical disorders. Vol. 1 and 2. 695 pp. Boston: Little, Brown & Co., 1939. $7.50.

The fact that these two volumes appeared in England over three years ago does not detract from their value, the essence of which is concise practical summaries of the treatment in most of the major medical disorders by distinguished English clinicians, many of them well known in this country. The directions for nursing care, diet, general management and convalescence, as well as the use of drugs, are detailed and specific.

A satisfactory feature is to find actual prescriptions written out. It is too bad that many proprietary names are used and that references are to the British *Pharmacopoeia*. This is inconsistent with the practical and otherwise time-saving features of the editing. Though specific, some of us may question the scientific basis for certain of the prescriptions. Nevertheless, one cannot but admire the therapeutic faith of one author who suggests for hemoptysis in mitral stenosis that the coagulability of the blood may be diminished by one teaspoonful, three times a day, of an aqueous solution containing sodium citrate and tincture of orange peel or by applying two or three leeches over the skin of the chest, and by giving a grapefruit every day.

One notices the references to treatment by manipulation, the employment of physical methods, spa treatment and climatotherapy. It seems to this reviewer that our accepted therapeutic efforts might be extended in these directions, though many of the spas and watering places mentioned in these volumes are now, unhappily, as unavailable to our English cousins as to ourselves.

One Hundred Thousand Days of Illness. Dorothy Ketcham. 477 pp. Ann Arbor: Edwards Brothers, Inc., 1939. $2.10.

Each year in the United States more than a million children are admitted to hospitals. This book traces in detail how the non-medical and social needs of these children have been met at the University Hospital, Ann Arbor, Michigan. The book is essentially an appraisal of the experience during hospitalization and subsequently of 275 patients during 100,000 days of illness over a sixteen-year interval (1922-1937). It describes in great detail, often with interesting photographs, the case work, occupational therapy, special activity and library service so well organized at the hospital in question.

The book should be of especial interest to hospital social-service workers and to the librarians of hospitals. It is attractively planographed, and the design for the interesting and unusual dust jacket was made by the children themselves using finger paints.

Obstetrical Practice. Alfred C. Beck. Second edition. 858 pp. Baltimore: Williams & Wilkins Co., 1939. $7.00.

The second edition of this excellent obstetric text has brought up to date the essential advances in the subject. The results of recent research in embryology and in the physiology of menstruation and lactation have been incorporated in appropriate chapters. The reviewer was particularly impressed by the interesting arrangement of recent information regarding the physiology of the placenta, especially placental interchange. Chapter 7 on changes in the maternal organism during pregnancy is especially well done; its arrangement is excellent, and the factual material is compendiously presented.

The author presents clinical problems and their treatment in a concise, clear and authoritative manner. There are over one thousand illustrations, many diagrammatic but all of them clear and pertinent to the subject matter.

This book is a valuable source of information for the undergraduate student and for the physician in general practice. While it is too brief to be used as a reference book by the obstetrician, it contains much recent material in which he will be interested.

Nutrition and Physical Degeneration: A comparison of primitive and modern diets and their effects. Weston A. Price. 431 pp. New York and London: Paul B. Hoeber, Inc., 1939. $5.00.

"Dr. Price has written," says Professor Earnest Hooton in his foreword, "what is often called 'a profoundly significant book.' The principal difference between Dr. Price's work and many others so labelled is that in the present instance the designation appears to be correct." With this estimate the reviewer wholeheartedly agrees. For basically simple as are Dr. Price's studies they are of fundamental importance, and his conclusions, taken at full implication, emerge as new and highly provocative of thought.

It has long been recognized that modern civilization has been attended by certain degenerative changes in man's body. Tooth decay is conspicuously rampant, together with severe malformation of the dental arches. Why should modern civilized man have such wretched teeth? Or conversely, why should his more primitive brother have such good ones? Dr. Price seems to have been the first to see that the answer to this second question might serve in great measure to answer the first. He set about to find it.

There exists a sufficiency of such primitive human material for study; scattered about the world are isolated remnants of primitive racial stocks still practically free from dental ills. Dr. Price studied groups in Switzerland, the Outer and Inner Hebrides, Alaska, parts of the United States and Canada, the islands of the south Pacific, eastern and central Africa, Australia and New Zealand, the Malay peninsula and the Amazon basin. He even investigated the ancient peoples of Peru and their descendants.

All these groups were studied in relation to their own blood relatives (when existent) who had adopted the white man's diet, as well as the Whites themselves in the same or contiguous areas. Naturally, the diets of such scattered groups appeared to vary enormously; the Eskimo must eat very differently from say, the South Sea islander, and the man of the seashore from the dweller in mountain fastnesses. Yet there must be a common dietary factor, nutritional factor, if you prefer, which ensures, apart from all climatic and geographic circumstances, an almost perfect dental status. And that factor is, says Dr. Price, an extremely liberal content in the diet of "the fat-soluble activator group" of vitamins — a group, he thinks, much larger than we yet know anything about.

The most startling thing about Dr. Price's observations is that diet appears to be not merely an important but practically the sole determinant of sound teeth and regular dental arches. A mixed racial heredity — very frequently charged with a heavy responsibility — he thinks has nothing much to do with it; for the stocks which he studied, immediately on adopting the diet of modern civilized man, began to suffer from dental ills, and the very first generation born after the adoption showed invariably a high incidence not only of tooth decay but of dental malformations.

But though enough has been given here, it is hoped, to convey the importance of Dr. Price's work, no brief review can possibly do him justice. Emphatically he deserves a full reading by anybody who is concerned in any way with the scientific aspects of nutrition. Man needs to think; this book should make him.

Problems in Prison Psychiatry. J. G. Wilson and M. J. Pescor. 275 pp. Caldwell, Idaho: The Caxton Printers, Ltd., 1939. $3.00.

The application of psychiatric principles to the management of criminals has been a slow and at times discouraging task. Perhaps its greatest stimulus came when the United States Public Health Service undertook to set up psychiatric clinics in the federal prisons. This book presents briefly and clearly the story of the experiences of two of the pioneers in this undertaking. The introduction by Dr. Treadway starts us off with enthusiasm. The book is conservative and throughout constantly expresses that uncommonest of human qualities, common sense. The reader is continually conscious of the fact that the authors have been through the mill and have learned about prisoners and prisons from actual work.